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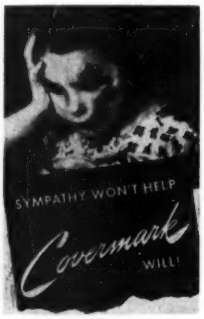

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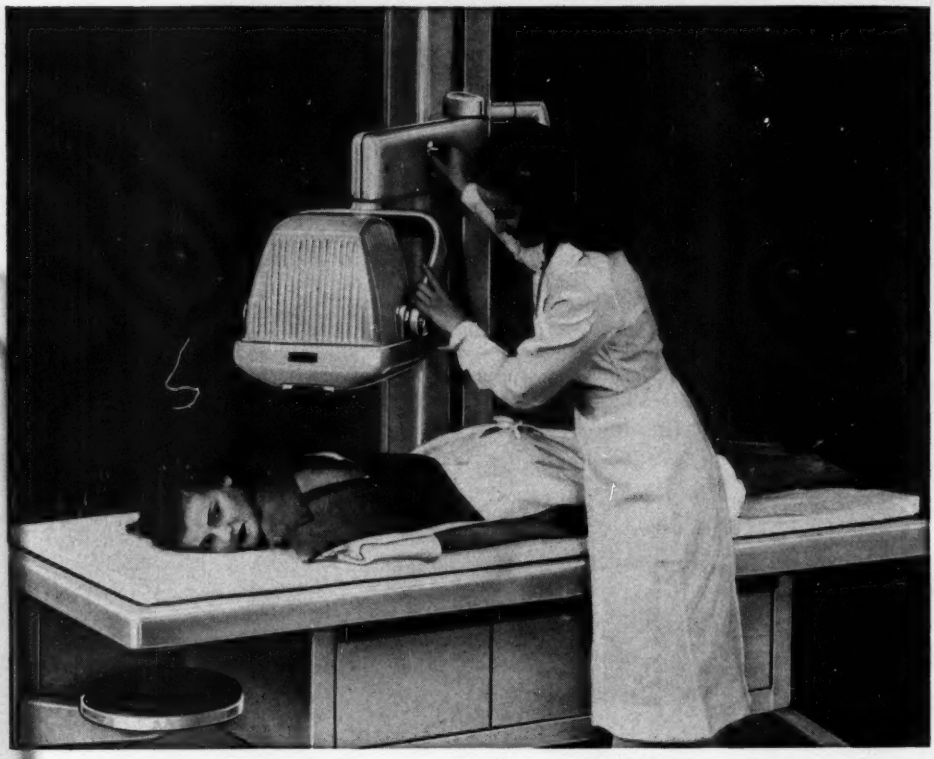

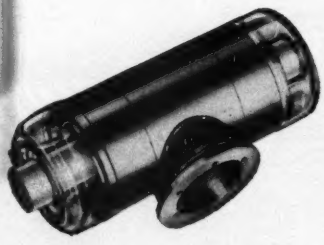

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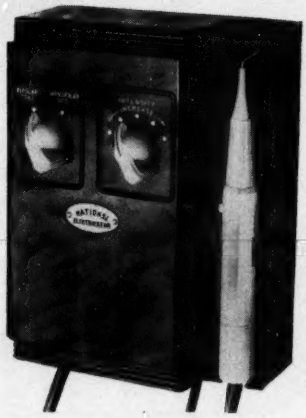

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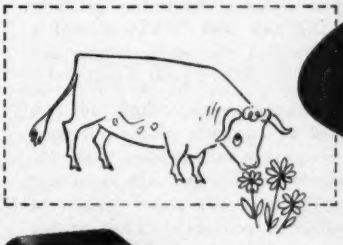

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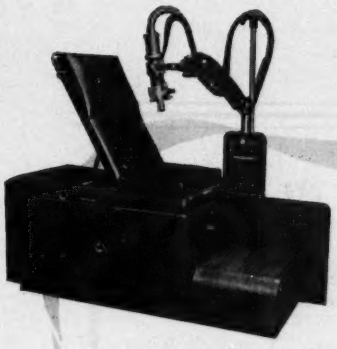

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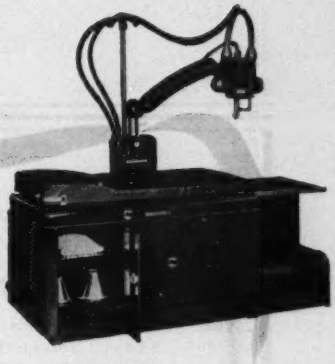

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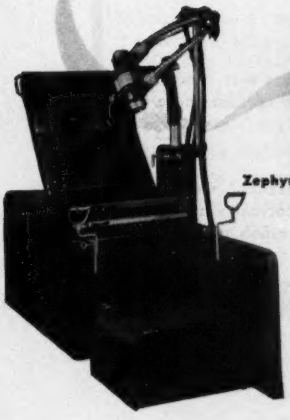

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CONTENTS

PAGE

Further Studies on the Mechanism of Adhesive Tape Dermatitis. SAMUEL M. PECK, M.D.; THEODORE J. MICHELFELDER, M.D., AND LAURENCE L. PALITZ, M.D., NEW YORK 289

Interstitial Radium Therapy: Description of a Short Intensive Technic. C. F. LEHMANN, M.D., AND J. L. PIPKIN, M.D., SAN ANTONIO, TEXAS 312

Early Prognosis of Lupus Erythematosus Discoides. THOMAS COCHRANE, B.Sc., CH.B., M.D., GLASGOW, SCOTLAND 323

Neutrophils Resembling L. E. Cells in Artificial Blisters. JOHN B. WATSON, M.D.; PAUL A. O'LEARY, M.D., AND MALCOLM M. HARGRAVES, M.D., ROCHESTER, MINN..... 328

Dermatitis and Secondary Leukoderma Due to Fabric-Lined Rubber Gloves: Report of a Case. I. BOTVINICK, M.D., DETROIT 334

Concurrent Infestation with a Rare Mite and Infection with a Common Dermatophyte. ALEXANDER A. FISHER, M.D.; ANDREW G. FRANKS, M.D., AND MAX WOLF, M.D., NEW YORK, AND MORRIS LEIDER, M.D., BROOKLYN 336

Rapid Permanent Staining and Mounting of Skin Scrapings and Hair. MORRIS A. GORDON, PH.D., ATLANTA, GA. 343

Histopathology of the Nodose Lesions of the Lower Extremities. L. H. WINER, M.D., BEVERLY HILLS, CALIF. 347

Seborrheic Keratosis and Verruca, with Special Reference to the Melanotic Variety. S. WILLIAM BECKER, M.D., CHICAGO 358

CLINICAL NOTES:

Polythionic Acid in the Therapy of Acne Vulgaris and Seborrheic Dermatitis. CLARK W. FINNERUD, M.D., AND J. MURRAY RIDDELL JR., M.D., CHICAGO 373

Oral Lesions in Pityriasis Rosea. MICHAEL G. ROSENBAUM, M.D., HAIFA, ISRAEL.. 376

Sex Hormone Sensitization (Corpus Luteum). W. H. GUY, M.D.; F. M. JACOB, M.D., AND W. B. GUY, M.D., PITTSBURGH 377

Tuberculosis Verrucosa Cutis Treated with Streptomycin. ARTHUR B. KERN, M.D., PROVIDENCE, R. I. 378

Subcutaneous Injections of Procaine Penicillin in Treatment of Chronic Sycosis Vulgaris and Hidradenitis Suppurativa Axillaris. MAURICE A. BELSON, M.D., NEW YORK 380

SOCIETY TRANSACTIONS:

Bronx Dermatological Society 383

Philadelphia Dermatological Society 392

Los Angeles Dermatological Society 401

San Francisco Dermatological Society 405

CORRESPONDENCE:

Letter from the German Dermatological Society Regarding the Death of Dr. Fred Wise 408

NEWS AND COMMENT 408

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Archives of Dermatology and Syphilology

VOLUME 63 MARCH 1951 NUMBER 3

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FURTHER STUDIES ON THE MECHANISM OF ADHESIVE TAPE DERMATITIS

SAMUEL M. PECK, M.D.
THEODORE J. MICHELFELDER, M.D.
AND
LAURENCE L. PALITZ, M.D.
NEW YORK

WE HAVE continued our studies on the mechanism of adhesive plaster dermatitis since our communication in 1948 on this subject.[1] We believe that the data which we are about to present, as well as the work of others which has appeared since that time, have added a great deal to our understanding of the factors involved in the dermatitis produced by adhesive tape.

Certain conclusions were drawn in our previous publication based on the data at hand at that time. Three types of adhesive tape irritation were described: (1) a relatively unimportant fleeting reaction which was mainly dependent on the tackiness of the adhesive mass (this reaction was believed to be due mainly to the mechanical trauma of removing the tape and could be decreased to a certain extent by the use of adhesive remover); (2) a reaction of sensitivity based on specific allergy to one or more of the ingredients in the adhesive (this was relatively rare), and (3) a third type, the one most frequently encountered, which developed in most instances only if the tape was left on for five days or longer and which was called the reaction of irritation.

The experiments which were reported indicated that when one adhesive tape produced a reaction of irritation and another did not in the same person there were differences in the p_H changes and the bacterial flora under the two adhesives. When the initial p_H of the skin surface was 5.2, under the irritating adhesive there was a relatively rapid rise to a final p_H of 6.3 at the end of seven days. The skin surface under the relatively less irritating adhesive showed a much slower rise in the p_H, and at the end of seven days it was 5.7. At the end of 14 days the p_H of the skin surface under the first adhesive was 6.7 while under the latter it was 6.4. The bacterial flora was altered quantitatively and qualitatively under both adhesives. However, the greater the degree of irritation, the greater the numbers of the bacteria found on the skin surface when the adhesive was removed. It was concluded, therefore, that the bacterial flora under the adhesive and probably the p_H played a role in the production of adhesive tape dermatitis.

From the Dermatologic Department, the Mount Sinai Hospital.

Read at the Seventieth Annual Meeting of the American Dermatological Association, Inc., Jasper National Park, Alberta, Canada, June 21, 1950.

1. Peck, S. M.; Rosenfeld, H.; Li, K. K., and Glick, A.: Mechanism of Adhesive Plaster Irritation, J. Invest. Dermat. **10**:367 (May) 1948.

Gaul and Underwood [2] were unable to substantiate the observations that the incorporation of bactericidal substances in the adhesive mass tended to decrease the incidence of the adhesive tape dermatitis. These authors did not parallel the work with p_H determinations and bacterial studies but based their conclusions entirely on the lack of differences in adhesive tape dermatitis observed when tape with and tape without fatty acid salts were applied simultaneously to the skin of the same person.

EXPERIMENTS

Materials and Methods.—Several brands of widely known adhesives were used in our study. We again used that brand of adhesive which we had referred to previously as hospital adhesive because it was found in previous experiments as well as in these about to be reported that it gave an unusually high incidence of reactions of irritation. There was also used an adhesive containing fatty acid salts and as a control the same adhesive without the fatty acid salts. Other brands of well known adhesives were used in several of the experiments and were found to be much less irritating than the hospital adhesive. We also tried a recently introduced brand of adhesive and found that it too produced an unusually high incidence of reactions of irritation.

Twenty biopsy specimens from 15 subjects served as a basis for our histological studies.

The method used for the study of the bacterial flora on the skin surface was that described by Pillsbury and Nichols [3] with some modifications. Instead of employing a swab technic for making the original cultures, we used a platinum spreader to obtain the material for culture. This change was necessary since the swab technic used by Pillsbury and Nichols introduced tiny particles of cotton which interfered with optical density readings. In order for bactericidal as well as bacteriostatic action to be evaluated, optical density readings were made at the end of 12 hours.

EXPERIMENT 1.—The histopathology of the various adhesive plaster reactions.

The Reaction of Sensitivity.—There were a number of biopsies made of specimens from patients exhibiting typical reactions of sensitivity to various brands of adhesive, including that containing the fatty acid salts.

Clinical Picture: The reaction of sensitivity is easily discernible clinically. Once sensitivity to one or more ingredients of an adhesive tape is present, a reaction can be seen on any part of the body with the exception of those covered by thick keratin layers in from 24 to 48 hours after the application of the tape. The clinical observations are those of an allergic contact dermatitis. The severity of the reaction depends on the degree of sensitivity. The reaction will vary from an intense edema and erythema with pruritus and scattered vesicle formation to intense vesiculation covering the whole area of application of the adhesive tape and even spreading beyond the borders of the site of application (fig. 1).

Microscopic Observations: A composite picture of a number of biopsy specimens of typical contact dermatitis due to adhesives clearly reveals that the histology conforms generally to that for other types of allergic contact dermatitis. There are mild hyperkeratosis, intracellular edema and spongiosis and the formation of intraepidermal vesicles throughout the epidermis. There is fairly heavy lymphocytic and some leukocytic infiltration around the dilated superficial vessels,

2. Gaul, L. E., and Underwood, G. B.: The Failure of Fatty Acid Salts to Lessen Cutaneous Irritation Caused by Adhesive Plaster, J. Invest. Dermat. **12**:173 (March) 1949.

3. Pillsbury, D. M., and Nichols, A. C.: Bacterial Flora of the Normal and Infected Skin: An Evaluation of Various Methods of Performing Skin Cultures, J. Invest. Dermat. **7**:365 (Dec.) 1946.

and the upper part of the cutis shows varying degrees of edema. In as little as 24 to 48 hours there is already an indication of beginning swelling of the ostiums of the sweat ducts in some sections. This is not part of the pathology of the allergic reaction but belongs to the reaction of irritation. There is little or no inflammatory reaction around the sweat ducts. Neither the vesicle formation nor the spongiosis has any relation in its distribution to the sweat ducts or follicular openings (fig. 2).

The Reaction of Removal.—Clinical Picture: Immediately after removal of the adhesive there may be seen varying amounts of diffuse erythema and edema. Such a reaction may disappear relatively quickly and can be diminished by the use of adhesive tape removers.[4] The reaction of removal is best seen when a good tacky adhesive is used. This may be evident when the adhesive tape is left on for only 24 to 48 hours. When it is left on for periods longer than five days some of the minor clinical characteristics of the reaction of irritation (probably due to the production of a miliaria rubra) may also be evident. In most instances a reaction of removal is superimposed or intimately mixed with a reaction of irritation.

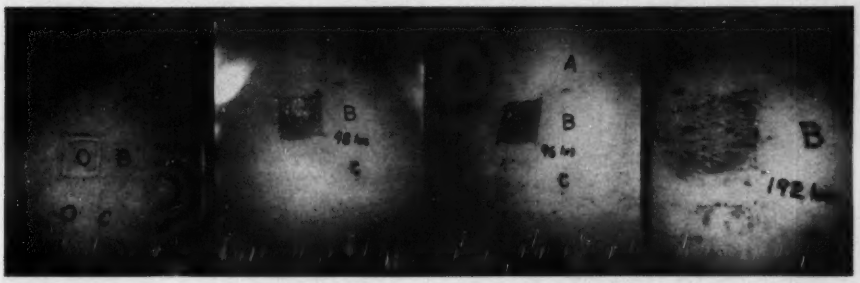

Fig. 1.—Reaction of sensitivity. Three different tapes—*A*, *B* and *C*—were placed on normal skin and left on for 24 hours. A reaction of sensitivity, which gradually increased in intensity and was still present at the end of 192 hours, can be seen at the site of application of tape, *B*. At *C* there can be seen a delayed allergic reaction.

Microscopic Observations: The epidermal changes were negligible. When a tape had been left on for only 24 to 48 hours and there was a relatively pronounced degree of erythema and edema clinically, very little of this was found on histological examination. The upper part of the cutis usually showed only a few dilated vessels with a slight perivascular infiltration of lymphocytes around them. There was moderate edema in the cutis. If the tape was left on for five days or longer without the clinical development of any degree of irritation there was always seen some beginning plugging of the ostiums of the sweat ducts. This will be discussed in detail when the histology of the reaction of irritation is described. In sections over which the tape had been left on only 24 to 48 hours, only swelling of the keratin at the ostiums of the sweat ducts was present (fig. 3).

The Reaction of Irritation.—Clinical Observations: The reaction of irritation always had some of the clinical characteristics mentioned with regard to the reaction

4. Glick, A. W.; Weissberg, G., and Peck, S. M.: A New Adhesive Tape Remover of Particular Value in Patch Testing, J. Invest. Dermat. **10**:399 (Jan.) 1948.

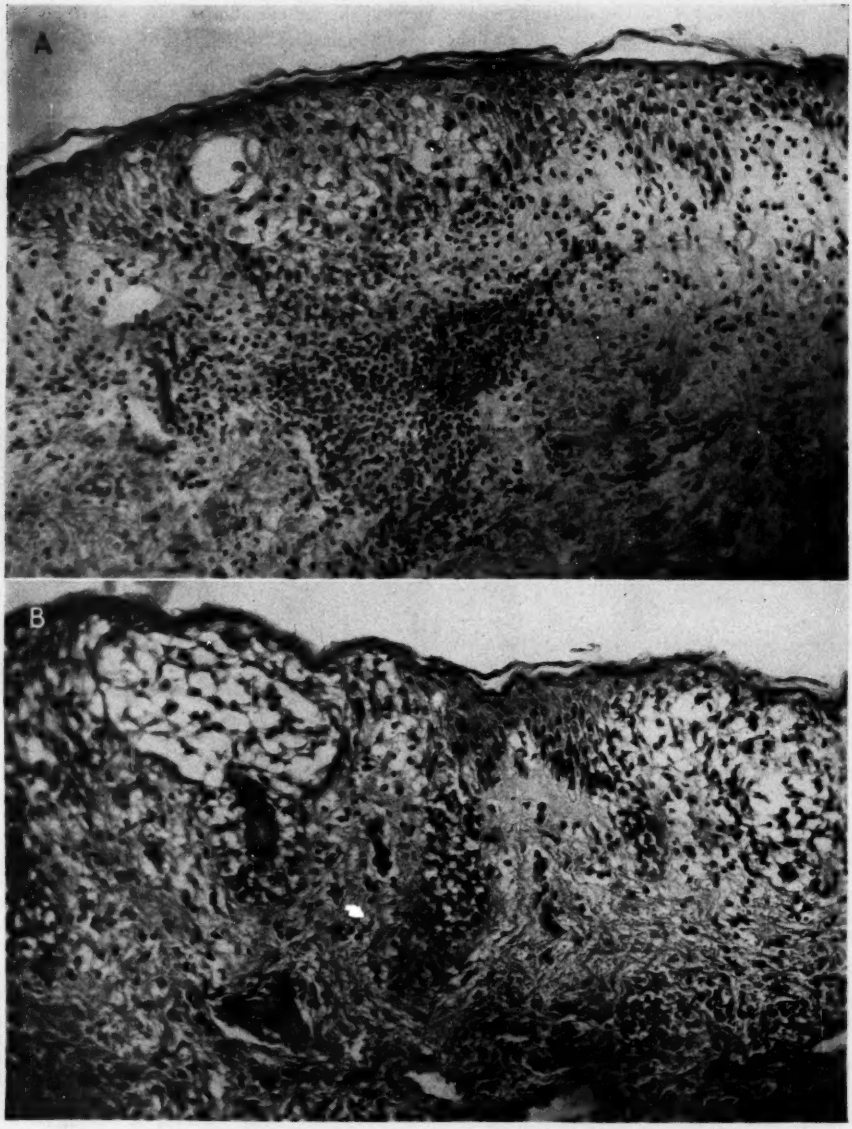

Fig. 2.—*A*, the histological features of a typical reaction of sensitivity. There is seen acanthosis, hyperkeratosis, diffuse spongiosis, intracellular edema and vesicle formation. The vesicles are in no relationship to hair follicles of sweat ducts. The inflammatory reaction here is much more intense than in any section from a reaction of irritation or removal. *B*, a higher magnification photograph of the reaction of sensitivity from another patient. There is demonstrated here intense vesicle formation, which bears no relationship to sweat duct distribution. A number of polymorphonuclear cells and eosinophils are seen invading the epidermis and are found in the vesicles.

of removal. It was usually seen after the adhesive had been left on five days or longer, but histologically changes may be observed when the adhesive is left on for only three days or even less if it will produce irritation after longer application. It was characterized primarily by varying numbers of erythematous papules which in their distribution had no relation to follicular openings. These papules might be on a general background of erythema and edema. Pruritus was usually present. When the reaction was more intense the papules were increased in number and so closely aggregated that they formed irregular patches. Vesicles were not seen, in contradistinction to the picture in the reaction of sensitization, but the surface of these closely aggregated papules was wet and oozed. In rare instances pustules

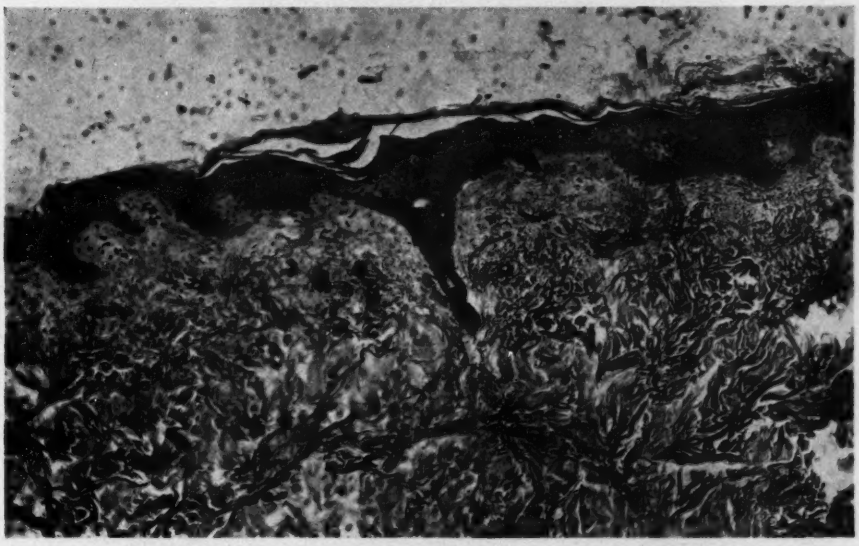

Fig. 3.—Over-all picture of the reaction of removal, showing very little inflammatory reaction in the cutis. There is early plugging of the ostiums of the sweat ducts. This is really part of the reaction of irritation. Clinically, there was no evidence of irritation as yet.

were present. However, we had the impression that some of these pustules seemed to be localized near follicular openings although some seemed to be in the vicinity of sweat ducts. Also characteristic was a slimy deposit on the skin when there was a pronounced reaction of irritation. Not infrequently the slimy deposit had a foul odor. This oozing was absent under adhesive tapes containing the fatty acid salts (fig. 4).

All other factors being equal, some tapes seemed to have an unusual tendency to produce the reaction of irritation after being left on the skin five days or longer. This was not a sensitivity reaction since it could readily been seen that, even when it was pronounced, reapplication of the same adhesive tape on the same person on another part of the body for 24 to 48 hours caused no reaction. There seemed

to be materials incorporated in the adhesive mass of some tapes which either by an action of mild but cumulative primary irritation or by a special tendency to produce miliaria-rubra-like reactions tended to produce this irritation with more uniformity than did the components of other tapes. By and large, the intensity of the reaction of irritation in the same person with the same tape varied with the time of

Fig. 4.—Varying reactions of irritation produced by three different tapes applied for seven days. The central area, *B*, shows minimal reaction produced by an adhesive tape in which fatty acid salts were incorporated. Above, at *A*, there was applied the same adhesive tape except that it did not contain fatty acid salts. Below was applied a recently introduced adhesive tape with a high index of irritation (not sensitization). The reaction was characterized by wetness and oozing on the surface, which have been described as characteristic of the pronounced reaction of irritation.

the year and the heat and humidity present and the degree of sweating. Such a reaction, unlike the reaction of sensitivity, usually began to subside promptly with the

removal of the adhesive tape and usually did not spread beyond the confines of the site of application.

Microscopic Observations: The most important and consistent observation in the pathology of this reaction was the mechanical blockage of the sweat ducts and the production of an experimental miliaria, as has already been indicated by Shelley and Horvath.[5] Even when there was relatively little dermatitis seen clinically, if a tape was left on for three days or longer changes related to the miliaria production could be noted (fig. 5, *A*). The severer the reaction of irritation, the greater the number of sweat ducts involved in any one microscopic field and the greater degree of involvement of the individual sweat ducts. However, the degree of inflammatory reaction in the cutis which was noted in some persons could not be explained on the basis of the changes in the sweat ducts alone. Usually, when the tape had been left on for less than five days or when the reaction was mild, the beginning changes consisted in narrowing of the ostiums of the sweat ducts as a result of swelling of the keratin. This then progressed to an actual plugging of the sweat ducts not only by swelling but also apparently by increase of the amount of keratin. There were seen inflammatory changes around sweat ducts and beginning dilation of the ducts in as little as 48 hours after application when a decidedly irritating adhesive was used. Clinically, practically nothing was evident. Such a tape as that just mentioned after longer application gave rise to a pronounced reaction of irritation. There was usually hyperkeratosis of mild degree throughout the section. As a result of the plugging of the sweat ducts by the keratin there was a dilatation of the intraepidermal portion of the duct below the plug. In some instances local areas of edema in the epidermis to the point of microscopic vesicle formation could be seen confined to the area of the dilated sweat duct. While no vesicles were seen around hair follicles, plugging of the follicular openings with keratin could also be seen in some instances. Hyperkeratosis of the follicular openings was noted usually when the adhesive tape was left on for seven days or longer (figs. 5 *B*, 6 and 7 *A*).

Acanthosis was seen especially in the vicinity of the plugged sweat ducts. The cutis in the immediate vicinity of such plugged ducts had a number of dilated and congested small vessels with mainly lymphocytic perivascular infiltration. The cutis itself was somewhat edematous, and lymphocytes and some polymorphonuclear leukocytes invaded the epidermis in the immediate vicinity of the dilated ducts. Such changes were often confined solely to the vicinity of the affected sweat ducts with no significant involvement of the rest of the epidermis and the cutis. In decidedly advanced cases of irritation, the inflammatory infiltrate was much heavier and the invasion of the epidermis by the lymphocytes and leukocytes was more pronounced. Also, the reaction was not confined so closely to the vicinity of the sweat ducts.

When histological examination was made of the two areas showing differing degrees of irritation, the one showing the more intense irritation in some instances may have had approximately the same number of ducts involved and the same

5. Shelley, W. B., and Horvath, P. N.: Experimental Miliaria in Man: II. Production of Sweat Retention Anidrosis and Miliaria Crystallina by Various Kinds of Injury, J. Invest. Dermat. **14**:9 (Jan.) 1950.

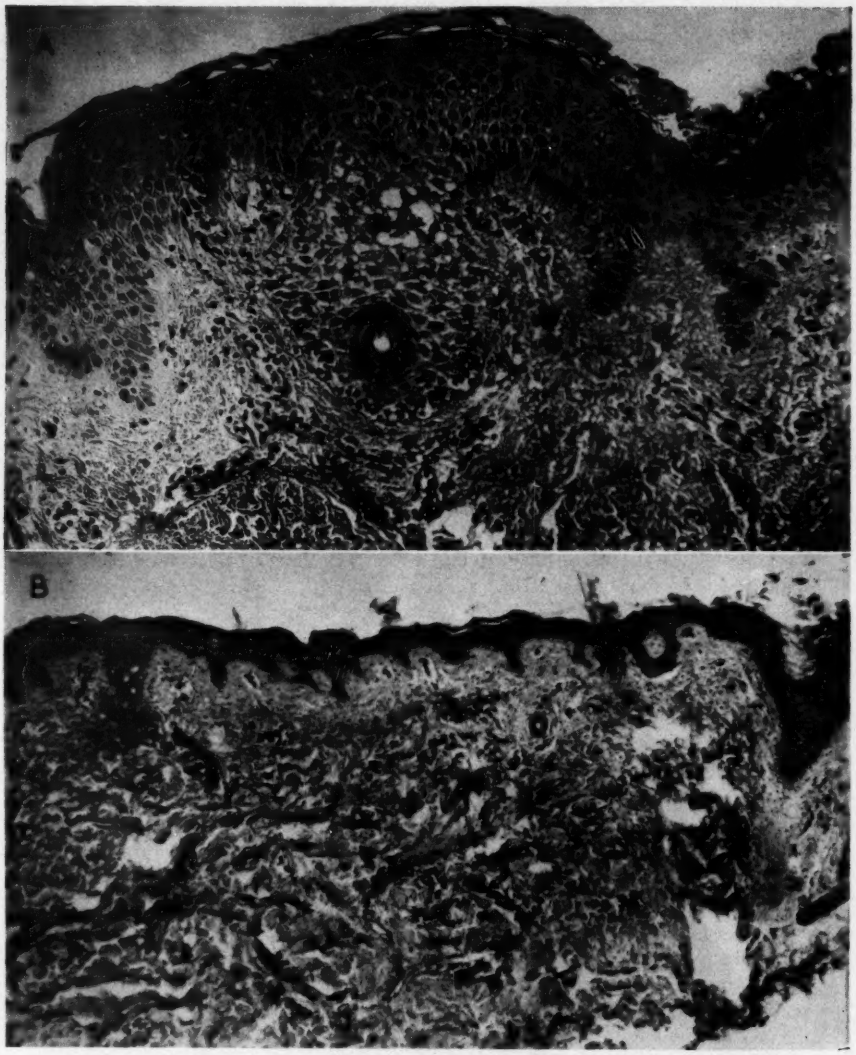

Fig. 5.—*A*, early changes of irritation in the vicinity of the sweat duct after 48 hours of adhesive tape application. This picture represents the beginning of plugging of the sweat duct. The reaction was found under adhesive which after application of seven days or longer produced a pronounced reaction of irritation (hospital adhesive). Early vesicle formation in the vicinity of a sweat duct can be seen. The blood vessels below the duct are dilated and show lymphocytic perivascular infiltration. There is invasion of the epidermis with lymphocytes. *B*, microscopic picture of a mild reaction of irritation produced by the adhesive without the fatty acid salts, which was left on for 10 days. There are seen not only plugging of the sweat ducts with accompanying mild inflammatory reaction but also generalized hyperkeratosis with definite plugging of the hair follicles.

degree of plugging of the sweat ducts but also had in the cutis a greater amount of inflammatory reaction which was not always related to sweat ducts. In such sections the superficial blood vessels showing dilatation and perivascular infiltration were greater in number and were not confined so closely to the vicinity of sweat ducts.

There are several distinct impressions to be gained from the microscopic observations of the sections from areas of irritation. There was no doubt that the plugging of the ostiums of the sweat duct and the production of a miliaria-rubra-like reaction constitute a basic part of the reaction and, perhaps, one of the most important mechanisms in the reaction of irritation. However, we could not help but feel that

Fig. 6.—Over-all picture of a section from a mild reaction of irritation produced by fatty acid-containing adhesive left on for 10 days. There is definite plugging of the sweat ducts with some surrounding edema of the intraepidermal portion of the duct and beginning vesicle formation. Note that the remainder of the epidermis is normal.

this was not the only factor because in a number of instances in corresponding sections the amount of plugging of the sweat ducts appeared to be the same and even the severity of the inflammations around and in the vicinity of the sweat ducts was about the same but there were differences in the intensity of the inflammatory reaction in the other parts of the sections. When such differences were seen they were not related to changes in the sweat ducts or hair follicles. They consisted primarily in vary degrees of inflammatory reactions in the cutis immediately below the epidermis (fig. 7 *B*). Essentially, in the one section there was a greater number of dilated superficial vessels. The perivascular infiltration around such vessels was greater, and in some instances there was even some invasion of the epidermis by

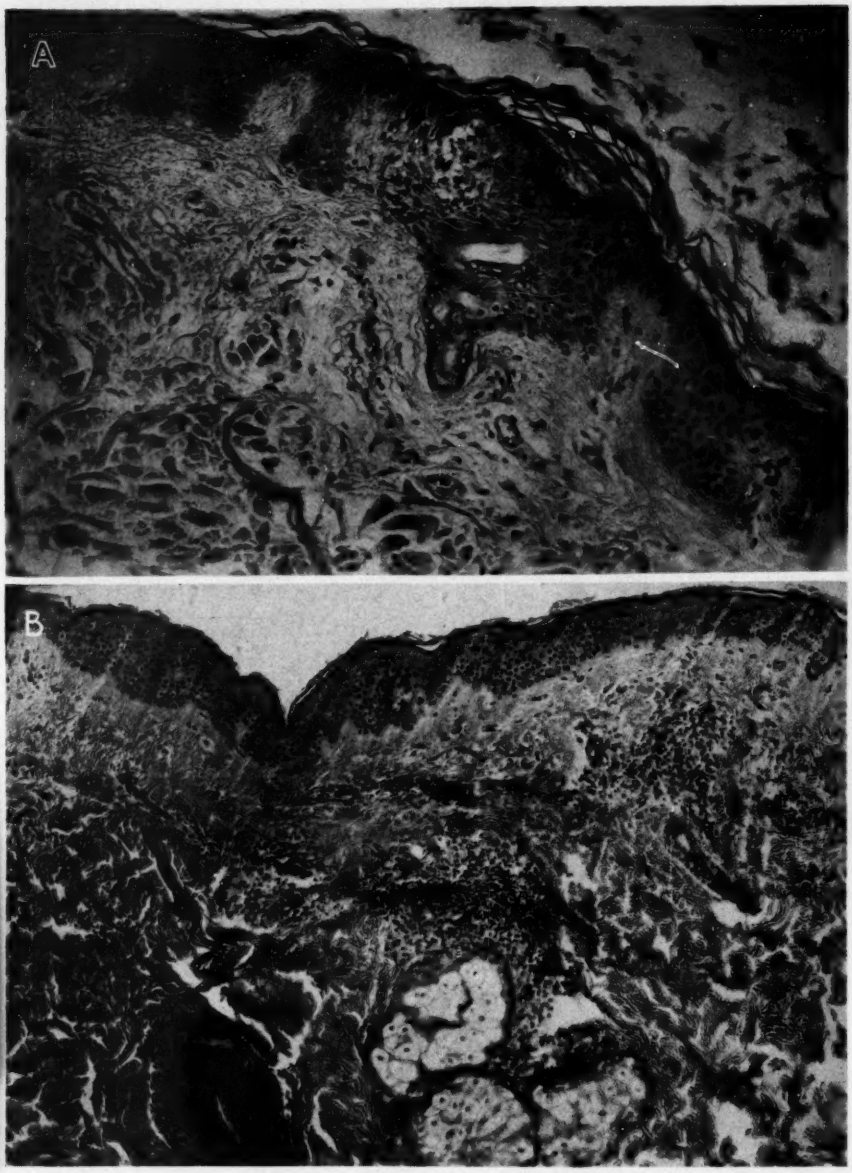

Fig. 7.—*A*, a high power view showing the reaction around the sweat duct in figure 6. *B*, microscopic section from an area of pronounced irritation after 10 days of application of hospital adhesive. There are a decided inflammatory reaction in the upper portion of the cutis, vascular dilatation and congestion, perivascular infiltration and moderate inflammatory reaction confined to a hair follicle in the midcutis.

lymphocytes without any direct relationship to any sweat ducts or hair follicles. It was in such types of reaction that we believed bacteria probably played a role.

EXPERIMENT 2.—In our previous publication, the work seemed to indicate that the incorporation of a fatty acid salt in the adhesive tape mass played a role in the reduction of the dermatitis by decreasing the numbers of bacteria under the adhesive tape. In an attempt to study further the role of bacteria in the reaction of irritation we carried out the following experiment. An adhesive strip in which the adhesive mass contained fatty acid salts was applied to the normal skin of the back, and a little distance below it another strip, without any fatty acid salts in its formulation, was applied. These were left on for 10 days and then removed.

Both of the tapes adhered well. The skin under that containing the fatty acid salts showed a mild erythema with scattered papules. The skin under the adhesive tape without the fatty acid salts differed in that the erythema was more pronounced and there was more of a maculopapular eruption.

Biopsies were made of specimens from each area.

Microscopic Observations.—It was noted that in both sections there was relatively the same amount of plugging of the sweat ducts; the only difference noted was that in the area covered by the adhesive containing the fatty acid salts there was a less intense reaction of inflammatory type as compared with the condition observed in the area covered by the tape not containing the fatty acid salts. The more intense reaction was characterized by greater dilatation and congestion of the superficial vessels with some perivascular infiltration. It is well illustrated in figures 8 and 9. It is the type of study just outlined which led us to believe that factors other than plugging of the sweat ducts contributed to the dermatitis following application of adhesive tape.

EXPERIMENT 3.—Adhesive tapes with and without fatty acid salts but otherwise having the same formulation of the adhesive mass were applied to the normal skin of the back. They were left on for 14 days and then removed. Immediately after their removal some irritation was seen under both adhesive tapes; it was more pronounced under the tape without the fatty acids. The differing degree of irritation consisted in a greater degree of maculopapular eruption and a more intense erythema.

A solution of iodine, castor oil and alcohol was painted over the area of the back where the adhesives had been applied as well as on the normal skin between and allowed to dry. Soluble starch was then dusted over both areas. Sweating was induced in the patients by the administration of 20 grains (1.2 Gm.) of acetylsalicylic acid and exposure to a heat element. It can be seen from figure 10 in the center of the photograph that in the presence of moisture the starch-iodine reaction takes place and is characterized by the black dots seen in the picture. It was noted in the experiment that there was decrease of sweating in both of the areas where the adhesive tape had been applied, whether the tape contained fatty acids or not. No pronounced differences in the degree of diminution of sweating could be noted between the two adhesives. Under both adhesives sweating was decidedly diminished as compared with the control area.

This experiment seemed to indicate that the difference in degree of dermatitis could not be accounted for by the plugging of the sweat ducts alone and the pro-

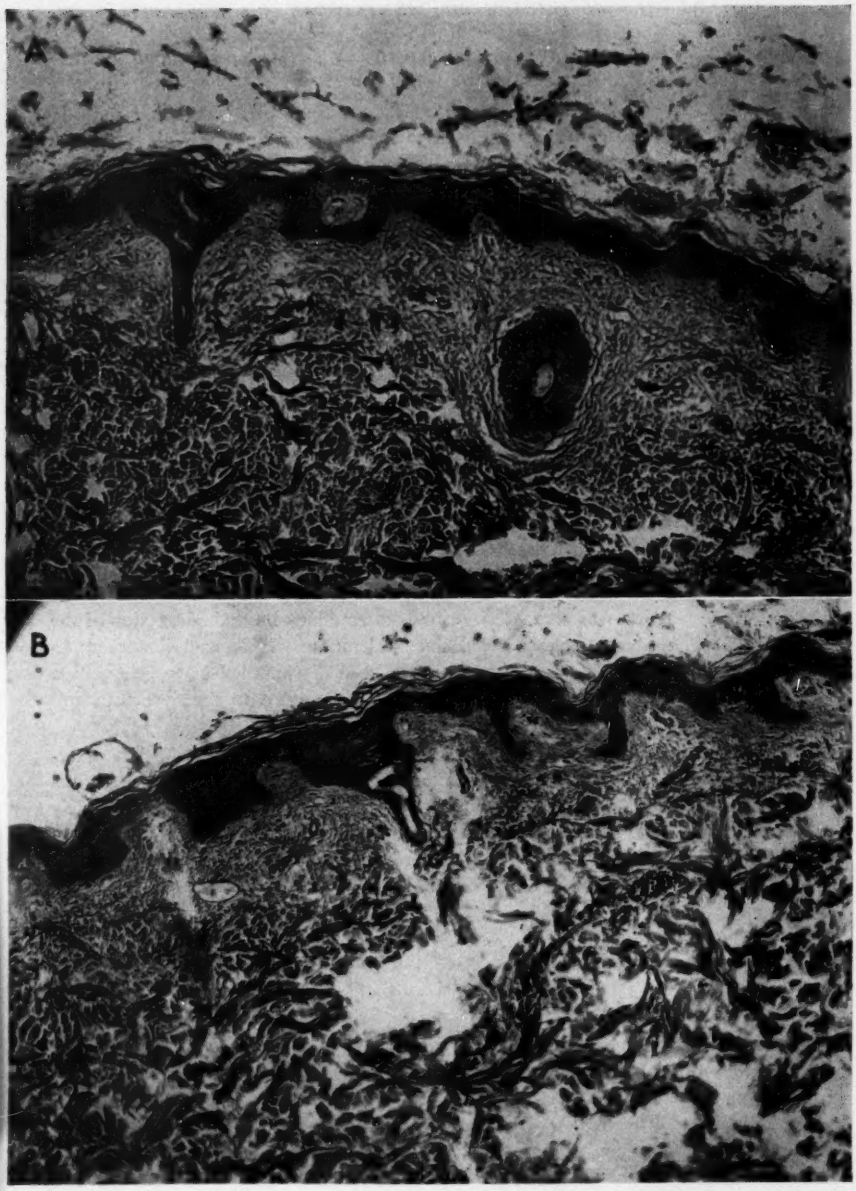

Fig. 8.—*A*, microscopic picture in a reaction of irritation produced by fatty acid-containing adhesive left on for 10 days. There is seen generalized hyperkeratosis, plugging of the sweat ducts with keratin and dilatation of the sweat duct below the plug. There is a sparse inflammatory infiltration or reaction in the papillary body in the vicinity of the plugged duct, with some perivascular infiltration. *B*, another field from the same section showing extreme dilatation of a sweat duct with sparse perivascular infiltrate.

duction of a miliaria-like reaction, especially since histological studies of such sites revealed that there was no pronounced difference between the two areas in the number and degree of swelling of sweat ducts in the epidermis.

EXPERIMENT 4.—Immediately after removal of the adhesives in the above-mentioned experiment cultures were made of the skin over the areas where both tapes had been applied as well as of the normal skin. At the end of 12 hours optical density studies were made. Aerobic and anaerobic cultures were made as in the previous experiment.

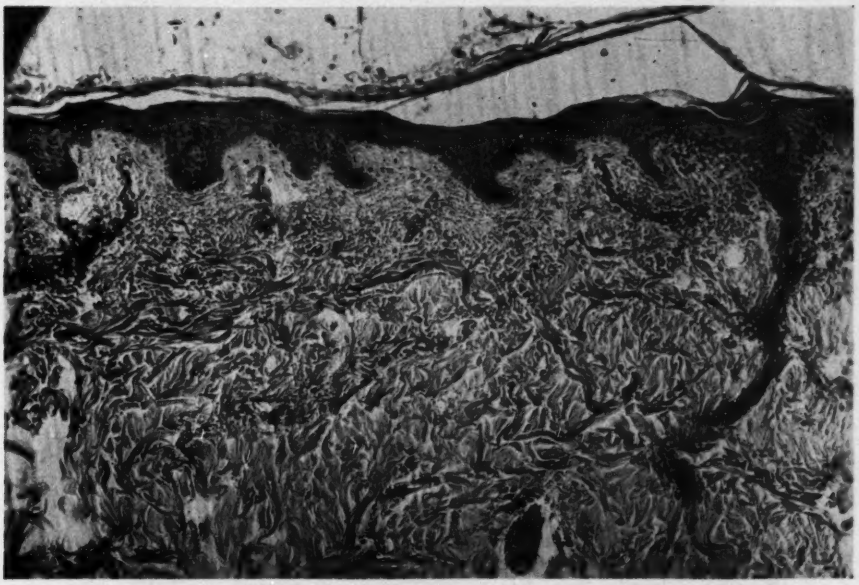

Fig. 9.—The specimen shown in this photomicrograph was also taken from a reaction of irritation produced in the same patient as in figure 8. In the area from which it was taken there was placed on the back for 10 days the same adhesive tape formula as described under figure 8, without the fatty acid salts. The difference in the resulting microscopic picture lies mainly in the degree of inflammatory reaction. A plugged sweat duct can be seen, and there is a more pronounced inflammatory infiltrate in the vicinity of the sweat duct. There are more dilated and congested vessels, and there is a more pronounced perivascular infiltration.

TABLE 1.—*Effect on Skin Bacteria of Incorporation of Fatty Acid Salts in Adhesive Tape Formula*

	24 Hour Aerobic Culture (Plain Nutrient Broth)	Optical Density	48 Hour Anaerobic Culture (Liver Tubes)	Optical Density
Normal skin	Sarcina, Staphylococcus albus, Corynebacterium	0.7	Staph. albus	0.4
Skin on which adhesive plus fatty acid salts had been left 14 days	Micrococcus	0.2	Staph. albus	0.1
Skin on which same adhesive without fatty acid salts had been left 14 days	Corynebacterium, gram-positive spore-forming bacilli, Micrococcus	0.4	Bacillus subtilis	0.5

It can be seen from table 1 that the numbers of bacteria were decreased in the area under the adhesive containing the fatty acid salts both as compared with the control areas and as compared with the areas under the adhesive without fatty acid salts. We can conclude from such an experiment that the incorporation of the fatty

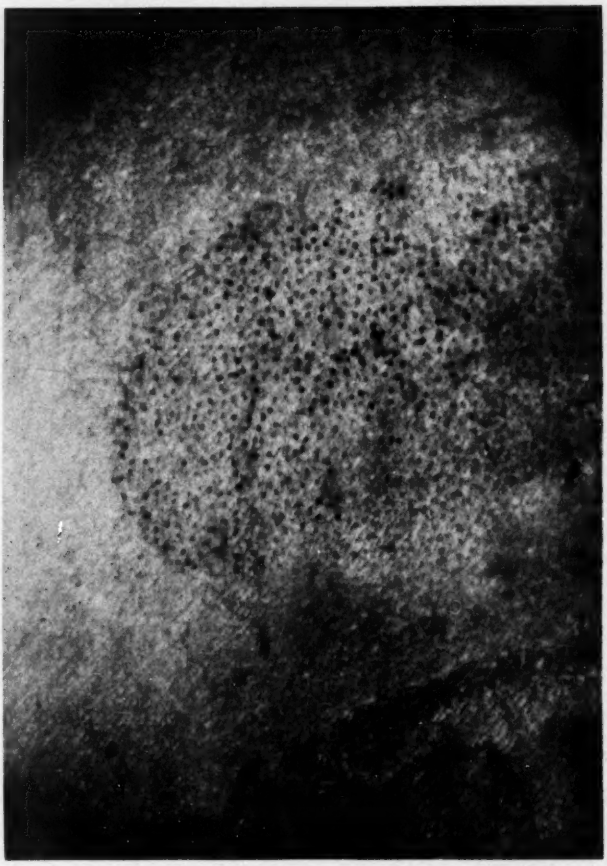

Fig. 10.—In the center of the photograph can be seen closely aggregated black dots indicating a starch-iodine reaction and showing that there was active sweating. Above and below it the reaction cannot be demonstrated, this fact showing the plugging of the sweat ducts by fatty-acid-containing adhesive tape above the active area of sweating and by the same formula without fatty acid salts below it.

acid salts in the adhesive mass certainly decreased the numbers of the bacteria on the skin surface under the tape.

EXPERIMENT 5.—In a further attempt to evaluate the possible role of bacteria as contributing to the adhesive tape dermatitis the following experiment was carried out.

The hospital adhesive which was known to produce a fairly consistent degree of irritation was used in this experiment. A fatty acid solution (solution sopronol* propionate-caprylate compound, a dilute *n*-propyl alcohol solution containing 12.3 per cent sodium propionate, 2.7 per cent propionic acid, 10 per cent sodium capry-

Fig. 11.—The numbers *1, 2* and *3* in the upper portion of the picture refer to reactions produced by (*1*) adhesive with fatty acid salts, (*2*) the same adhesive without fatty acid salts and (*3*) hospital adhesive of an entirely different formulation. All the adhesives were left on for 10 days. It is easy to see the differences in the amount of irritation produced. At *4* there was a reaction produced by the same hospital adhesive as at *3*, but there had been previous treatment of the skin by eight applications of fatty acid solution for four days (experiment 5), after which the adhesives were left on for 10 days. The reduction in the amount of irritation is evident.

late and 0.1 per cent dioctyl sodium sulfosuccinate) was applied twice daily, morning and evening, over the whole right side of the patient's back. After the second application had been allowed to dry, a strip of hospital adhesive tape was applied to

the skin of the back. Strips of hospital adhesives were applied daily, one below the other, for four successive applications, so that the first adhesive strip was placed over an area of the skin that had had two applications of the fatty acid solution; the second, over the area that had had 4 applications; the third, over that with six, and the fourth, over that with eight. Each adhesive strip was then left on for seven days. Aerobic and anaerobic cultures were made as previously described, and the optical densities of the bacteria cultured were determined at the end of 12 hours.

It can be seen from table 2 that the bacterial flora was progressively decreased by the application of the fatty acid solution. At the same time, there was a certain amount of diminution of the degree of irritation as compared with a control area (fig. 11).

We attempted to indicate the different degrees of irritation by means of colored photographs. We found that, unless such photographs were all taken on the same day, color photography did not bring out the different shades of intense erythema well. Here the different degrees of irritation were characterized not so much by a differing number of the papular reactions previously described as characteristic of

TABLE 2.—*Effect of Multiple Application of Fatty Acids* on Skin Bacteria Under Adhesive Tape†*

Total Number of Applications	24 Hour Aerobic Culture (Plain Nutrient Broth)	Optical Density	48 Hour Anaerobic Culture (Liver Tubes)	Optical Density	Amount of Adhesive Tape Irritation
2 (first day)	Micrococcus	0.5	Micrococcus	0.5	Pronounced
4 (second day)	Micrococcus	0.2	Staph. albus	0.15	Less pronounced
6 (third day)	No growth	0.0	Staph. albus	0.1	Less pronounced
			Coryne-bacterium		
8 (fourth day)	No growth	0.0	Micrococcus	0.05	Least irritation

* Solution sopronol ® propionate-caprylate compound was used.
† Hospital adhesive tape left on for seven days before cultures were made.

the production of miliaria as by a lessening of the diffuse erythema and edema and especially the production of oozing and sliminess (fig. 4).

DISCUSSION

The reaction of sensitivity to adhesive tape represents such a typical example of allergic contact dermatitis both clinically and microscopically that it needs but little discussion. However, success in an attempt to trace the specific sensitizing ingredients responsible for this reaction is practically impossible.

Schwartz and Peck [6] in 1935 attempted to trace the ingredients in adhesive tape mainly responsible for the allergic reactions to the particular adhesive tape which they studied. Patients exhibiting reactions of sensitivity were given patch tests with dammar resin, shellac, mastic, sandarac, rosin, elemi, turpentine oleoresin and Burgundy pitch.

It was concluded that the resins and the smoke-cured wild rubber were the agents chiefly responsible for the reactions. These authors, too, however, noted reactions of dermatitis to adhesive plaster without being able to obtain a positive reaction to patch tests with all the ingredients supposed to have gone into the adhesive plaster

6. Schwartz, L., and Peck, S. M.: Irritants in Adhesive Plaster, Pub. Health Rep. **50** (no. 24):811 (June 14) 1935.

formula. Undoubtedly they were dealing with reactions of irritation which were not recognized as such at that time.

During the several years of our study we communicated with a number of manufacturers in an effort to obtain the various ingredients in adhesive plaster. We gratefully acknowledge the cooperation of Johnson & Johnson, the Elastoplast Corporation and the Seamless Rubber Company. The following list of ingredients was furnished us so that we could carry out patch test studies in patients exhibiting reactions of sensitivity to the adhesive tapes from the aforementioned manufacturers:

Santovar 0
Vistac #1
Vistanex B-100
Zinc oxide
Paragon clay
Titanium dioxide (Titanox A)
Primol D
Staybelite ester #10
Piccolyte S-115 (petroleum residue resin)
Suprex clay
Amberex B
Hydrated alumina C-730
Factice R
Hydratex clay
Galex NXD
Starch
Stalite (isoheptene and β-Naphthylamine)
Aralex (sorbitol solution)
Lanolin (hydrous wool fat)
Wool fat
Natural rubber (pale crepe rubber, Pará rubber)
Hydrogenated resins
Synthetic rubber GRS
Agerite (monobenzyl ether of hydroquinone)
Pitch
Petrolatum
Texas A white oil
Beeswax

In instances of sensitivity to the three plasters mentioned above, we tested the patients with the individual ingredients as furnished by the manufacturers, but in no one instance were we able to obtain positive reactions. Unfortunately, the manufacturer whose adhesive tape produced the greatest number of reactions of sensitivity as well as reactions of irritation did not cooperate with us, so that we could not test the majority of our patients with reactions of sensitivity.

The observations that we obtained, i. e., negative patch test reactions with the ingredients supposed to represent all the materials in the adhesive tape, were similar to those in the experience of others.[7]

7. Gaul, L. E., and Underwood, G. B.: Primary Irritants and Sensitizers Used in Fabrication of Footwear, Arch. Dermat. & Syph. **60**:649 (Nov.) 1949. Grolnick, M. S.: Studies in Contact Dermatitis: I. Adhesive Plaster Dermatitis: Techniques for Surface Testing on Patients Sensitive to Adhesive Plaster, J. Allergy **7**:341 (May) 1936. II. Adhesive Plaster Dermatitis: Clinical and Immunologic Observations on Patients Sensitive to Adhesive Plaster, ibid. **7**:556 (Sept.) 1936; Factors Involved in the Production of Adhesive Plaster Irritation, Am. J. Surg. **50**:63 (Oct.) 1940.

It has been pointed out [8] that the chemical nature of several of the ingredients frequently used in the manufacture of adhesive masses is such as to make some variation from batch to batch likely and absolute chemical control difficult except within certain relatively broad limits. This, plus the likelihood that chemical mutation compounds or systems are present in the completely formulated mass which differ in reactivity from the respective basic ingredients, demands the utmost circumspection in the evaluation of reactions to adhesive tape of any type.

The commonest type of adhesive tape dermatitis encountered was that referred to as the reaction of irritation. The etiological factors responsible for this reaction are most interesting and are just now being better understood.

When we decided to carry out histological studies of the different types of adhesive plaster dermatitis we were stimulated by Sulzberger and his associates' fundamental research on sweating.[9] These authors described a sweat retention syndrome which was characterized by severe attacks of pruritus often associated with the rapid development of small shiny papules, papulovesicular lesions or vesicular lesions which depended on elevations of environmental temperature and relative humidity. Their observations led us to examine our sections for evidence of changes such as plugging of the sweat ducts. As can be seen from our histological studies, this plugging could readily be demonstrated in the reaction of irritation as a fundamental basic mechanism underlying the clinical and microscopic picture. While we were in the midst of this work, Shelley and Horvath [5] reported their observations in which they reproduced the sweat retention syndrome by means of adhesive tape, among other methods. The photomicrographs which we are presenting duplicate very closely the photographs published by Shelley and his associates [10] and Sulzberger and his co-workers [9] in their experimental production of miliaria rubra.

Apparently there is a consistent microscopic reaction when an adhesive tape is left on the skin for three days or longer. The degree and extent of the reaction varies appreciably with differing adhesive tapes. It can be regarded only in part as the reaction of the sweat apparatus alone to any tacky material remaining on the skin for any length of time and plugging the ostiums of the ducts. The ingredients in the adhesive must play an important role in producing plugging of the ducts, or there would not be such pronounced differences between various adhesives in producing this phenomenon.

8. Henderson, J. (Medical Director, Johnson & Johnson): Personal communication to the authors, July 11, 1950.

9. (*a*) Sulzberger, M. B.; Zimmerman, H. N., and Emerson, K., Jr.: Tropical Anhidrotic Asthenia (Thermogenic Anhidrosis) and Its Relationship to Prickly Heat, J. Invest. Dermat. **7**:153 (Aug.) 1946. (*b*) Sulzberger, M. B.; Zak, F. G., and Hermann, F.: Studies of Sweating: II. On the Mechanism of Action of Local Antiperspirants, Arch. Dermat. & Syph. **60**:404 (Sept.) 1949. (*c*) Sulzberger, M. B.; Hermann, F.; Keller, R., and Pisha, B. V.: Studies of Sweating: III. Experimental Factors Influencing the Function of the Ducts, J. Invest. Dermat. **14**:91 (Feb.) 1950.

10. (*a*) Shelley and Horvath.[5] (*b*) Shelley, W. B.; Horvath, P. N.; Weidman, F. D., and Pillsbury, D. M.: Experimental Miliaria in Man: I. Production of Sweat Retention Anidrosis and Vesicles by Means of Iontophoresis, J. Invest. Dermat. **4**:275 (Oct.) 1948. (*c*) Shelley, W. B., and Horvath, P. N.: Experimental Miliaria in Man: III. Production of Miliaria Rubra (Prickly Heat), ibid. **14**:193 (March) 1950.

If we analyze the histology of the reaction of irritation we see that the plugging of the ducts is due primarily to hyperkeratosis. This is not limited to the sweat ducts alone but can be seen throughout the slide; even follicular hyperkeratosis is produced. The inflammatory reactions set up around the sweat ducts are due to the fact that the action of sweating forces the sweat through the thin wall of the duct. The ingredients of the sweat find their way into the surrounding epidermis and produce an inflammatory reaction. The inflammatory reaction produced will depend on the degree of plugging and the number of the sweat ducts that are plugged, on the activity of the sweating mechanism (relative humidity and temperature) and probably on the individual ingredients of the sweat and their relative irritating capacity. It is the plugging of the sweat ducts by hyperkeratosis which initiates the process.

O'Brien [11] showed that local application of wool fat increased excretion of eccrine sweat, and this observation could be confirmed by Sulzberger and his collaborators.[9b] The latter also were able to cause miliaria-rubra-like reactions by application of aluminum sulfate. However, in that particular report Sulzberger and co-workers noted that the aluminum salts, while causing an inflammatory reaction and thus blocking the ducts, did not produce actual narrowing of the lumen such as we noted in the histology of the reaction of irritation. In the further study by Sulzberger, Hermann, Keller and Pisha [9c] those authors were able to produce miliaria rubra by biologically electropositive substances and thus could reduce the outpouring of sweat. Biologically negative agents apparently tended to increase the outpouring of sweat.

Shelley and his associates [10b] produced changes closely resembling those found in miliaria crystallina by means of iontophoresis. Using either the anode or the cathode without any active ingredients other than tap water they were able to demonstrate plugging of the sweat ducts by means of hyperkeratotic and parakeratotic changes in the stratum corneum at the ostiums of the sweat ducts. Shelley and Horvath [12] also reported keratotic plugging at the openings of the sweat ducts after application of adhesive plaster from three to 10 days. Scotch® tape had less effect than ordinary adhesive tape. They could show that whatever vesicle formation was present histologically was actually due to pressure of the sweat behind such a plugged orifice because this formation could be inhibited by atropine. No intact vesicles were seen in the sections. Shelley and Horvath were able to produce similar changes by means of many other substances. The reaction of irritation due to adhesive tape resembled clinically in many of its elements the miliaria rubra experimentally produced by Shelley and Horvath.[10c] They described the appearance of discrete to confluent erythematous macules associated with small papules. This description is quite an accurate one of the basic change seen clinically in adhesive tape dermatitis without exposure of the patient to increased sweating.

The second type that Shelley and Horvath described, in which there were clear superficial vesicles with erythematous halos, was not seen by us as an adhesive tape dermatitis. Perhaps such reactions could have been induced had we induced profuse sweating in patients after longer applications of adhesive tape, just as Shelley and Horvath did in their experiments.

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11. O'Brien, J. P.: A Study of Miliaria Rubra, Tropical Anhidrosis and Anhidrotic Asthenia, Brit. J. Dermat. **59**:125, 1947.

12. Shelley and Horvath: Footnotes 5 and 10*c*.

In all instances these authors reported that the clinical changes developed on normal-appearing skin and only on the areas treated after 30 minutes to four hours of profuse sweating. This profuse sweating of course did not take place in the patients exhibiting adhesive tape dermatitis under normal conditions. In their third paper,[10c] Shelley and Horvath described microscopic changes which were similar regardless of whether they were produced by iontophoresis, aluminum chloride, adhesive tape or maceration. They saw hyperkeratotic and parakeratotic plugs and plaques of stratum corneum developed at the sweat duct orifices. The earliest abnormality consisted in the dilatation of the sweat duct in its terminal intraepidermal portion. Thereafter, edema and the lymphocytic infiltration appeared immediately underneath the affected ducts in the stratum corneum. These observations were quite consistent with the changes which we saw in the reaction of irritation due to adhesive. It was only in extreme cases of adhesive tape dermatitis that we saw the development of intraepidermal vesicles. This probably was due to the greater degree of sweating in that particular subject. Shelley and Horvath concluded that it was a nonspecific injury which was the basic mechanism in the production of the miliaria rubra and that this nonspecific injury to the epidermis often resulted in maceration.

All the previous discussion evidently points to the fact that the histology of adhesive tape dermatitis as represented by the reaction of irritation is primarily due to the same sort of mechanism which produces miliaria rubra. We believe that the plugging of the sweat ducts is not so nonspecific as the injuries discussed by Shelley, Horvath and Sulzberger, among others. Any sort of nonspecific injury causing swelling of the keratin at the ostiums of the sweat ducts would produce the reaction of miliaria rubra. This is not quite the explanation in its entirety as far as adhesive tape dermatitis is concerned. We believe that ingredients in the adhesive tape mass are partially if not primarily responsible for the production of the plugging. It is noted through many of the sections that there is a diffuse hyperkeratosis throughout the slide and not just at the ostiums of the sweat ducts; even follicular hyperkeratosis with plugging may be present.

Rubin [13] recently showed that hyperkeratosis could be reproduced just in response to continuous mechanical irritation such as could be expected under the slight movement of the adhesive tape mass over the skin. We believe with Shelley and associates that maceration may produce inflammatory changes at the ostiums of the sweat ducts but certainly does not tend to produce hyperkeratosis throughout the epidermis.

Examination of the ingredients incorporated into the adhesive tape might give us a clue. Certainly there is a cause other than tackiness and maceration under adhesive which can explain the constancy with which certain adhesive tape formulas produce pronounced degrees of irritation with changes leading to hyperkeratosis and plugging of the sweat ducts.

The publication of Schwartz and Peck [14] on occupational acne might give us a clue to the role of the ingredients of adhesive plaster in producing plugging of sweat ducts. In this publication it was shown that there are certain definite chem-

13. Rubin, L.: Hyperkeratosis in Response to Mechanical Irritation, J. Invest. Dermat. **13**:317 (Dec.) 1949.

14. Schwartz, L., and Peck, S. M.: Occupational Acne, New York State J. Med. **43**:1711 (Sept.) 1943.

ical substances which have a special tendency to produce hyperkeratosis by their keratogenic properties and that such chemicals may lead to plugging of the orifices of the sweat ducts and the hair follicles, the basic mechanism in occupational acne. Among such chemicals which were described were the insoluble cutting oils, coal tar, coal tar distillates, coal tar pitch, chlornaphthalenes, chlordiphenyls, solid chlorbenzoles and the chlorphenols. It is difficult to trace the composition of many of the actual ingredients in the adhesive tape mass because they are identified only by trade names, with secret composition. It might be worth while to investigate each individual ingredient from the standpoint of its special tendency to produce hyperkeratosis and thus plugging of the sweat ducts. Once this hyperkeratosis and plugging develop, all the sequelae necessary for production of miliaria rubra are present, as has been brought out by the previous authors.

Notwithstanding its importance, the concept of adhesive tape dermatitis of the nonallergic variety being primarily due to the formation of a miliaria-like reaction does not explain the complete picture of adhesive tape dermatitis. When several different tapes are placed on the skin and varying degrees of dermatitis are produced by them, it can be shown that the tape producing the severest dermatitis will have under it the greatest number of bacteria. This can be shown even with the same tape fairly consistently. When we examine such an observation in the light of the experiments which we have reported, it does not seem to us that the question of the role of bacteria in adhesive tape dermatitis can be dismissed lightly. It is not too difficult to concede that bacteria can multiply under adhesive tape when maceration is present. If it is admitted that p_H changes on the skin and the fatty acids in sweat play a role in controlling bacterial growth on the skin surface, then why is it so difficult to believe that the bacteria would tend to multiply when the very protective mechanism which prevents their multiplication is removed? It is, therefore, not surprising that the incorporation of bacteriostatic or bactericidal substances into the adhesive tape formula in the form of fatty acid salts should tend to decrease the number of bacteria under the adhesive tape.

Granted that the main role in the production of adhesive tape dermatitis is not played by the bacteria, we still have to explain the cause of the differing degrees of irritation produced by two different adhesives in the same person or the same adhesive in two or more persons when microscopically the amount of plugging of the sweat ducts seems to be the same. The sweat retention cannot be the entire explanation when the two different adhesives are placed close enough together on the same person so that difference in sweat ingredients can be held responsible for the difference in inflammatory reaction. Furthermore, when it is found that a factor such as decrease in bacterial flora on the skin surface is consistently found under the adhesive showing less irritation, then we must at least consider that the bacterial flora with or without accompanying p_H changes plays some role in the adhesive tape dermatitis. We concede, however, that perhaps the importance of the bacterial factor is not as great as was thought in our previous publication. The experiments reported in which an irritating adhesive tape such as hospital adhesive could be shown to effect a less severe reaction of irritation after previous treatment of the skin with bacteriostatic substances seems to us a further proof that the bacterial multiplication under adhesive does contribute to the inflammatory reaction.

We wish to point out that the wetness without vesiculation which is seen in pronounced cases of adhesive tape irritation is not found when bactericidal substances are incorporated in the adhesive tape mass.

SUMMARY AND CONCLUSIONS

Adhesive tape may produce an allergic contact dermatitis which is well characterized clinically and microscopically. This reaction is rare. It is practically impossible to trace the specific sensitizer in any adhesive because the chemical composition of the ingredients varies from batch to batch.

Adhesive tape can also produce a fleeting unimportant reaction which has been called the reaction of removal. This is due to mechanical removal of the tape, especially when a tacky adhesive has been used.

The majority of the cases of adhesive tape dermatitis are due to a specific mechanism which can be summarized as follows. The initiating factor in most instances, if not in all, is a plugging of the ostiums of the sweat ducts by keratin. The development of the sweat retention syndrome and the production of what might be referred to as a miliaria rubra follow. Everything else being equal, the degree of irritation developing is dependent on the number of sweat ducts involved and the extent of the plugging, on the activity of the sweat glands and probably on the relative irritating properties of the ingredients of sweat. The various adhesive tapes contain ingredients which tend to stimulate hyperkeratosis to more or less degree. Such a hyperkeratosis is not limited to the ostiums of the sweat ducts but is diffuse; even follicular hyperkeratosis may be produced. From this account it can be seen that, the differences depending on the formulation of the adhesive tape, some adhesive tapes may tend to irritate more than others. Once plugging of the sweat ducts takes place, the bacteria may multiply under the tape and add to the maceration and irritation.

ABSTRACT OF DISCUSSION

Dr. Hamnett A. Dixon, Toronto, Ontario, Canada: Dr. Samuel M. Peck's paper on the mechanism of adhesive tape dermatitis is most thorough—20½ double-spaced pages, tables, slides and 1½ pages of references on a subject that appeared so simple, namely, mechanical and chemical irritation.

The longer the plaster is in place, the more heat, moisture and maceration, or the more ideal the culture medium and hence the greater the bacterial growth. I do not think this finding should lead to the inference that the bacterial flora plays a major role, or a part, in the production of the dermatitis; rather, the more prolonged the irritation, the greater the bacterial growth. As the paper states, the intensity of irritation varies directly with heat, humidity and degree of sweating, and Dr. Peck notes that Gaul and Underwood were unable to substantiate the finding that bactericidal substances in the adhesive tape decrease the incidence of adhesive tape dermatitis.

In some parts of the microscopic specimen varying degrees of inflammatory reaction occurred immediately below the cutis without direct relation to sweat ducts or hair follicles. This reaction is thought to have been due to bacterial invasion. May it not have been due simply to the degree of irritation?

It is assumed that fatty acid salts in the adhesive lessen the degree of dermatitis by reducing the number of bacteria under the adhesive tape. May it not be that the dermatitis is less severe because fatty acid salt has acted as a neutralizer to an irritant or irritants in the adhesive?

In the aerobic culture Staphylococcus albus is not grown from the site covered by adhesive containing fatty acid salts nor is it grown from the site covered by adhesive free from fatty acid

salts. On an aerobic culture, however, Staph. albus is grown from the fatty-acid-containing adhesive site but is not grown from the site covered by tape free from fatty acid.

On the removal of adhesive tape applied after applications of fatty acid to the skin Staph. albus is not grown on aerobic culture but is grown on anaerobic culture from sites which received four and six applications of the fatty acid.

In conclusion Dr. Peck states that the dermatitis is due to plugging of the ostiums of the sweat glands by keratin, the degree of dermatitis depending on the number of sweat glands plugged, the irritant being partially or primarily ingredients in the adhesive mass.

I believe that the value of the paper—and it is an excellent one—lies in the pathological observations, namely, that the reaction of irritation produces a picture similar to miliaria rubra, which was so ably described by J. P. O'Brien, whose investigation of tropical anhidrosis began in 1945 and was published in April 1947.

DR. STEPHEN ROTHMAN, Chicago: I wonder whether in the pictures Dr. Peck has shown there is true hyperkeratosis or just swelling of the horny layer which promptly follows occlusion of the surface. It is a controversial point whether infection plays a role in adhesive tape dermatitis or not. It seems to me that in some cases infection may be quite significant; in others it may not be present.

DR. SAMUEL M. PECK, New York: I wish to thank the discussers for their valuable contribution to the problem which I tried to present. It is quite clear that Gaul and Underwood missed the point which I presented in our first paper, namely, that bacteria on the skin surface play a role, if not the most important role, in the adhesive tape dermatitis. It seems to me that in the paper which we have just presented the proper place of bacteria in the production of the miliaria-like reaction has been better established. I believe, however, that skin bacteria play a secondary role rather than a primary one in initiating the dermatitis.

If Dr. Rothman were able to study our microscopic sections, he would be able to see that the picture was of a true hyperkeratosis but that earlier swelling did occur. A further point which I wish to stress is that this hyperkeratosis is greatly influenced by the ingredients in the adhesive plaster mass. It is in this respect that manufacturers after proper research could improve their products.

INTERSTITIAL RADIUM THERAPY

Description of a Short Intensive Technic

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AND
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FOR MANY years the method described herein of treating superficial carcinoma of the skin has been used by us satisfactorily, and we think that it is worthy of consideration. We shall refer to it as the short intensive treatment in distinction from the long, low intensity method of interstitial radium therapy. Before describing the short intensive method and discussing its results, we shall discuss briefly the long treatment.

LONG LOW INTENSITY TREATMENT

In 1929 Cade [1] reported on the advantages of using a small amount of radium, over a long time (168 hours), with a filter of 0.5 mm. of platinum (or more), using gamma rays. He stressed the fact that such a technic had a selective effect; that is, it killed the cancer cell and did not injure normal tissue enough to leave objectionable sequelae. From the time of his reports interstitial radium therapy was gradually standardized to the use of filtration of 0.5 mm. of platinum or more (which filtration takes out all beta rays). Further progress in standardization of radium dosages was made by Friedrich, Glasser, Mautz, Gray, Maynford, Paterson and Parker, Quimby, Sievert, Failla, Marinelli and others.[2]

The mathematical method of determining dosage has as its basis a unit of intensity rather than a unit of dose. Unit intensity is defined as the intensity of the radiations at a distance of one cm. from one mgm. point source of radium element (in equilibrium with its products) filtered by 0.5 mm. platinum. This has been called the intensity millicurie (IMc.), and the dose delivered in one hour at the point in question is referred to as one intensity-millicurie-hour (IMc-hr.). Therefore, if full details are available, it is theoretically possible to calculate the intensity in IMc. at any desired point.[3]

It is now agreed that the average output of 1 mg. of radium from a point source, filtered through 0.5 mm. of platinum, will deliver, at 1 cm., approximately 8 gamma roentgens in one hour.

Read at the Seventieth Annual Meeting of the American Dermatological Association, Inc., Jasper National Park, Alberta, Canada, June 21, 1950.

1. Cade, S.: Radium Treatment of Cancer, New York, William Wood & Company, 1929.

2. Glasser, O.; Quimby, E. H.; Taylor, L. S., and Weatherwax, H. L.: Physical Foundations of Radiology, New York, Paul B. Hoeber, Inc., 1947, p. 317.

3. Cade, S.: Malignant Disease and Its Treatment by Radium, ed. 2, Baltimore, Williams & Wilkins Company, 1948, vol. 1, p. 43.

Paterson and Parker[4] have given the following list of biologic effects of various radium doses on normal, healthy skin (when dosage is continuous over a period of eight days or, if intermittent, lasting at least 12 hours in each 24):

3,000 gamma-roentgens—faint erythema

4,500 gamma-roentgens—definite erythema

6,500 gamma-roentgens—moist desquamation—"radiodermatitis"; the reaction lasts about six weeks, but return to normal is complete

7,500 gamma-roentgens—a very pronounced reaction of similar type, lasting for a longer period and borderline for safety.

Doses that are lethal to cancer cells are variable with the type and location of the cancer. Small squamous cell cancers of the skin can be successfully eradicated with a dose of 2,600 gamma roentgens. Ebenius,[5] with his technic (using 10 mg. needles and filtration with an equivalent of 0.5 mm. of platinum, interstitially), cures cancer of the lip with doses of 2,250 to 2,600 gamma roentgens. Widman,[6] using contact therapy with capsules, used 6 to 10 threshold erythema dose (T.E.D.) and has cured small lesions of the lip with 6 T.E.D. (1 T.E.D.-1,000 gamma roentgens).

SHORT INTENSIVE TREATMENT

The needles used in the short intensive treatment contain 10 mg. of radium element in the form of the sulfate, are 19 mm. long, 1.3 mm. in diameter and have a wall thickness of 0.3 mm. of platinum. The rays passing through that filter are composed of 9 per cent beta rays and 91 per cent gamma rays.[7] There is no reliable means of expressing beta radiation mathematically as gamma roentgens are measured.

These needles are placed interstitially, usually, in a single plane at the base of the lesion in most instances. They are arranged in the following ways: (1) in a triangle, about the borders of small lesions; (2) in parallel rows, unless the central two thirds of the needle does not approximate 3 mm. distance from the border of the desired field of radiation, in which instance another insertion is made at the right angle in the border of the lesion, and (3) in a rectangle or hexagon (rarely)—if more than four needles are thus arranged, needles are placed in the center of the lesion 5 mm. apart.

The distribution of them varies with the intensity desired. We have learned that if we want a very intensive dose we should place them as close as 3 mm. apart (between needle walls). Where a radiation-sensitive tumor is treated, we may use distance between the needles as much as 5 mm. Our aim is to get as selective effect as possible so as not to leave radiation scars that are so thin and

4. Paterson, R., and Parker, H. M.: A Dosage System for Gamma Ray Therapy, Brit. J. Radiol. **7**:592-632 (Oct.) 1934.

5. Ebenius, B.: Cancer of Lip: A Clinical Study of 778 Cases with Particular Regard to Predisposing Factors and Treatment with Radium, Acta Radiol., 1943, supp. 48, pp. 1-232.

6. Widman, B. P.: Cancer of the Lip, Am. J. Roentgenol. **63**:13-25 (Jan.) 1950.

7. Stenstrom, W.; Quinby, A. H., and Pendergrass, E. P.: Report of the Research and Standardization Committee of the American Radium Society, Am. J. Roentgenol. **43**:118-125 (Jan.) 1940.

atrophic as to break down from slightest use. Such poor results would also be obtained by our leaving the needles in longer. We have learned that the optimum time for such insertions is 2½ hours.

Procaine hydrochloride 2 per cent is used as anesthetic. Cook's dental syringe is used since its small needle (25 gage) facilitates anesthesia in a small area with very little trauma. A wheal is first made by intradermal injection around the area, and then the solution is placed under the lesion. It is not infrequent for the cancerous tissue to be defined by the procaine infiltration, since it will "pop" and not distend as normal skin will when infiltrated. The anesthesia is almost immediate. This method calls for very little solution and distends the tissue to a minimum. Effort is made to inject toward the center upward of the lesion,

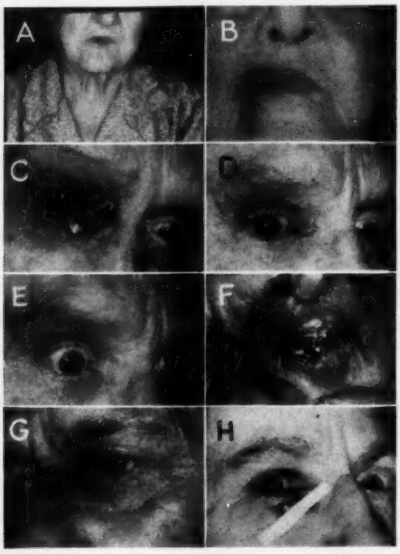

Fig. 1.—*A*, patient aged 84, with recurrence at edge of scar 14 years after interstitial radium therapy, re-treated with seven needles for 2½ hours. *B*, result after four months. *C*, needles in cancer of canthus. Note shields. *D*, reaction after three weeks. *E*, result after one month. *F*, two needles in epithelioma of lower eyelid. *G*, result after three months. *H*, shields, 1 mm. of lead, under ends of needles.

thereby reducing the possibility of pushing cancer cells out of the field to be treated.

This technic has served us well in treating all small carcinomas of the face (eyelids, canthi, nose and lip included). Since the needles are only 19 mm. long, they can be easily inserted in concave sites of the skin, such as the canthus area and the nasomaxillary fold. Their short length and thin wall make them easily adaptable to treating cancers of the eyelid and other small lesions in cases in which a good cosmetic result is desired.

The short time allows a completion of treatment on an outpatient status (with no hospitalization) in one trip and is a convenience to patients who have to travel long distances, as some of ours do.

TYPES OF LESIONS TREATED

Most of the lesions treated by this method are basal cell carcinomas. Very large lesions are usually treated by other means, totally or adjunctively. The majority of the lesions on the face which are treated this way do not usually measure over 1.5 cm. in their longest diameter. The needles are usually placed in one plane and arranged to radiate intensively the base of the lesion.

We are convinced that the location of the cancer on the skin determines to some degree its radiation sensitiveness, besides its grading. The explanation may lie in what is referred to as the "cancer bed." For instance, practically all early lip cancers, although squamous cell, respond satisfactorily to the described technic. But those on the back of the hand and posterior portion of the neck are likely to be recalcitrant (regardless of their type or grading). It is very rare indeed to fail in treating an early lesion on the eyelids.

Good results could be obtained with surgical treatment and other means in most of the types of cases in which the technic is applied. However, there are especial instances wherein interstitial radium therapy seems to be the method of choice. This will be apparent when we discuss treatment in special locations.

CANCER OF EYELIDS

The eyelids constitute a location where a selective effect is most desirable. A plastic repair of an eyelid is most difficult and never entirely satisfactory. Interstitial radium therapy is particularly valuable here. The needle or needles are inserted at the base of the lesion. The surrounding tissue is protected by small strips of lead 1 mm. thick, which are placed under the projecting ends of the needles and on top of the lesion. A gold-plated eyeshield is placed in the conjunctival sac to help protect the lens from any radiation. The ensuing reaction is thus confined to the area within the shield, which fact indicates that it is the beta radiation that is chiefly effective in this technic (an effective dose of gamma radiation on the cancer could not be shielded close with this small thickness of lead). There is a minimal amount of objectionable sequelae—the treated skin is not excessively atrophic, and permanent loss of eyelashes is confined to a very small area. We never expect a blockage of the lacrimal ducts unless the cancerous induration envelops the duct.

We feel that the fear of radiation around the eyes causing cataracts needs revision. We have seen yearly a 57 year old man who had one of these needles inserted in the conjunctiva near the limbus under the base of a papilloma (grade 1) for 2½ hours in 1937. The reaction was intense. There is no sign of a cataract. On the other hand, we have seen cataracts occur years after heavy radiation with hard rays given around the eyes. A case in point is that of a Mexican boy, now aged 13, who had a total dosage of 5,800 (effective wavelength, 1 mm. copper half-value layer) to a large chrondrosarcoma of his nasal and glabellar region at the age of 3.

We feel that this short intensive method of radium therapy is less likely to produce cataract than the more prolonged method of interstitial radium, since the latter spreads a bigger dose over a wider area and consequently irradiates the lens system more intensively. However, if one shields well with plenty of lead the chances of radiation cataract can be reduced to the point that it is a minor

hazard. We are now following for the twenty-fifth year a man who had 7,000 gamma roentgens applied to the inner canthus and inner fourth of upper and lower eyelids by contact technic for a fairly well advanced basal cell cancer. In his treatment 3 mm. of lead was used to shield the eye. His eye at the age of 62 is still clear, with 20/20 vision (fig. 2 *A*). This case was reported by one of us in 1931.[8] In that report are cited 15 cases that had been followed for three years, and 58 cases followed for five years or more. In all these cases radium had been used with the short intensive method for eyelid cancer, and in none had cataract developed. Since that time we have been alert in following up cases from this standpoint and have not yet seen a cataract ascribable to this short technic.

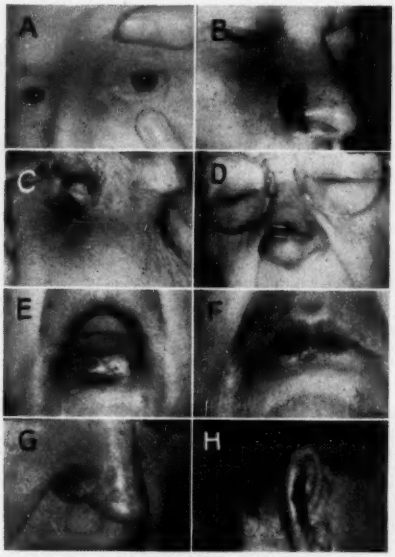

Fig. 2.—*A*, result 22 years after treatment with 8,000 gamma roentgens (radium pack) to inner canthus. No cataract. *B*, four needles in two planes. *C*, one needle at right angle to others. *D*, needles in "iceberg" cancer of nose. *E*, grade 2 cancer with leukoplakia, biopsy scar. *F*, result after one month. *G*, atrophy, eight years after the use of five needles over the tip of the nose for 2½ hours. *H*, atrophy, eight years after treatment with four needles.

CANCER OF THE NOSE

Early cancer of the nose should never offer any doubt of curability by any of the accepted methods. The interstitial short treatment gives a selective effect in early cases, and a result can be obtained that leaves hardly any atrophy and no deformity. Sometimes one encounters what has been described as an "iceberg" cancer. This is one in which the macroscopic part is elevated and clinically characteristic but the major extension is in and under the skin around the central elevation. One has to be on the lookout for these on the nose (particularly at the nasolabial junction). One runs a better chance of getting these lesions by inter-

8. Lehmann, C. F.: Epithelioma of Eyelid, Texas State J. Med. **27**:422-426 (Oct.) 1931.

stitial radiation than by firing at them at right angles to the skin through portals that shield too close up to the macroscopic pathologic features. To avoid insufficiently radiating this type we always include in the radiated field any adjacent area that exhibits telangiectasis or a dyskeratotic appearance.

CANCER OF THE LIP

The majority of cancers of the lower lip are highly differentiated, which observation, generally speaking, indicates radiation resistance. Ackermann and del Regata,[9] in a series of 248 cases, report 66 per cent grade 1, 20 per cent grade 2, 2 per cent grade 3 and 11 per cent ungraded. Yet the majority of early lesions are curable (95 per cent).[10]

Ebenius had a cure rate of 94.8 per cent in small superficial lesions in the age group below 49, with his technic (different from ours) of interstitial radiation, using needles of 5 and 10 mg. strength, with filtration with the equivalent of 0.5 mm. of platinum, in situ three to four hours. (In large lesions he used needles containing 3 and 6 mg. of radium, total length 20 to 30 mm., left in place 16 hours.) His relative cure rate in small superficially growing primary tumors in the age group above 70 was 48.6 per cent. The interstitial use of radium is an ideal method of treatment since it does not require hospitalization and leaves the normal configuration of the lip. The short treatment is applicable to most, but not all, of the early lip cancers. An infiltrating, ulcerative cancer with induration of more than 1 cm. had best be treated with other technics, such as needles containing 0.66 mg. of radium per centimeter length, with filtration of 0.5 mm. of platinum for 168 hours; or with Ebenius' method; or with roentgen radiation, or by surgical means (unless the growth is a very anaplastic one). On the other hand, an exophytic type of growth, or a verrucous one, of high differentiation, can be safely handled by the short routine.

We occasionally treat moderately advanced lesions that require insertion of the needles in more than one plane, but the majority of our patients have been treated with a distribution of the needles in a single plane. Our cases of lip cancer have been classified as early, moderately advanced and well advanced. Lesions of 0.5 cm. diameter or less are classed as early, regardless of the patient's statement of the duration. The moderately advanced include those up to 1.5 cm. Early metastasis of lip cancer is very rare. When adenopathy is present, dissection of the glands is not advised until the primary tumor is healed unless the primary lesion is nonulcerative and there is every reason to believe that the enlarged glands are noninflammatory. Our statistics are not complete, and a later report will deal with them in detail. Cure of early lesions is achieved in approximately 98 per cent.

PRECANCEROUS LESIONS OF THE LIP

Previous irritation of the lip is a factor in practically all cancer cases. Its expression may be either leukoplakia or chronic cheilitis actinica. The short interstitial technic of radium treatment is a very satisfactory method of clearing either of these conditions. Very thin leukoplakia that persists and is "irreversible" to

9. Ackermann, L. V., and del Regata, J. A.: Cancer: Diagnosis, Treatment, and Prognosis, St. Louis, C. V. Mosby Company, 1947.

10. Ackermann and del Regata,[9] p. 240.

normal, after protection from irritants of tobacco and sunlight, may be treated by cautery or electrodesiccation. But thick leukoplakia is more satisfactorily treated with radium because of the better cosmetic result.

SCARS

The atrophy that follows a heavy dose of radium sometimes leaves as troublesome a condition as the lesion which was treated. The skin in such cases is vulnerable to irritants; it may be tender or split easily. For that reason we should favor treatment that leaves as little atrophy as possible. In other words, the treatment should be selective: i. e., it should kill the cancer cell but leave as little untoward early or late sequelae as possible. Most of the patients whom we treat are outdoor workers whose lips and skin are severely affected with the well known strong sunlight in this area. The scars from this short treatment hold up as well as those from any other treatment, and, with moderate after-care, these patients do very well. We have had some instances in which postradiation ulcers have occurred, but they have been rare and are explained on the basis that the limits described for this technic were exceeded: (1) either the needles were spaced too close together, or (2) they were left in place too long, or (3) a recurrence was re-treated after original treatment which was either surgical excision or irradiation, either one of which leaves deficient vascular supply to the cancer bed. The postradiation ulcers usually heal, if small, but very deep ones have to be excised.

ADVANTAGES OF SHORT TIME TECHNIC

The advantages of the short time technic are as follows: (1) it is saving of the patient's time and allows distribution of radium to patients to a maximum efficiency, and (2) the cosmetic result is ideal.

When patients have an ambulatory status it is a distinct advantage to them as well as to the physician for the treatment to be administered on one visit. The cost of hospitalization as well as time out from work for hospital procedures are important considerations for most patients. The cost of travel back and forth is another, particularly for those patients who have long distances to travel to treatment centers. The short time technic also allows a minimum of time for the radium to be reserved per patient and allows for the distribution of radium expeditiously. (It is not infrequent for us to dispose of lesions in the morning and be ready to dispose of another group in the afternoon.) It might be said (in rebuttal) that no amount of expense or inconvenience is too much for one who wishes to get a proper cure of a cancer. That is true, but, everything else being equal, we believe that the short treatment deserves consideration for the above mentioned reasons. Also, it consumes only a few minutes of the operator's time—much less than that required for fractionated treatments with either radium or roentgen rays.

After our patients receive treatment they are given instructions regarding the reaction (an epithelitis that results in an eroded, exudative area the length of the needle), which appears in about two weeks, is at its height for about 10 days and then rapidly disappears. The skin erythema gradually disappears in from one to two months. The application of ammoniated mercury ointment, 5 per cent, is advised during the reaction. In about the third week of the reaction a thin

necrotic membrane covers the lesions. Frequently, when patients are available, this is curetted away and Monsell's solution, which dries the area, is applied; a dry scab forms thereafter. (The solution is not applied to the lip or eyelid.) Ordinarily the patient is not seen after the treatment for five or six weeks. Follow-up observations are requested twice more at two month intervals, and then yearly.

COSMETIC RESULTS

We believe that the cosmetic results following this treatment is comparable to that following interstitial radium therapy with the use of 0.5 mm. platinum filtration. There is no question in our minds that "quality" of radiation makes a difference in cancer cell response as well as in the effect on normal tissue. Comparisons of scars following the use of chiefly soft beta radiation (with the radium plaque) or soft roentgen rays (either being given in lethal cancer cell doses) with scars following the use of gamma radiation leave no question as to the following differences:

Scars from Softer Rays	Scars from Harder Rays (Gamma)
Old ones telangiectatic	Little telangiectasia except where doses have been tremendous
Occasional keratoses or reappearance of cancer in the atrophic skin	Rare to see keratoses or cancer appear
Scars sometimes so thin that plastic repair needed	Excision rarely needed

We are confident that the beta radiation in this technic (plus the relatively small gamma ray dose) gives sufficient intensity to give a lethal cancer cell dose in a small site in a relatively short time and yet gets this desired effect without the tissue's being overirradiated with beta rays. Confining such a desired dose to a very small area is advantageous in certain circumstances, such as when the lesion is on an eyelid or on a lip, to avoid radiation necrosis of the alveolar ridge, which sometimes follows heavy roentgen ray treatments or gamma radiation therapy.

Cancers in other sites for which this technic offers particular advantage are as follows: (1) Basal cell carcinoma in the concha of the auricle or in the auditory canal. (When the growth is discovered early, a cure is expected and this technic does not cause painful reactions in the ear drum which the use of heavy, more penetrating qualities of radiation does. However, we do not trust to it if lesions in the auricle are deep and extensive.) (2) Basal cell carcinoma at the auriculo-mastoid junction.

DISADVANTAGES OF THE SHORT INTENSIVE METHOD

The method we have described is not a technic that is standardized so that the intensity distribution in tissue can be mathematically determined and expressed in universal physical standards of dosages.

Another objection to the method might be that it exposes the operator and technicians unduly to radiation and is not suitable to ordinary office practice.

A recital of personal experience would probably be in order: One of us (C. F. L.) has handled radium (including tubes, needles and a half strength plaque) varying from 90 to 150 mg. since 1922, except for 4½ years in Army service. The other (J. L. P.) has handled the same amount continuously since 1927, but during the second world war his exposures were more frequent, since he

did double duty in this regard. J. L. P. has no local effect on his finger tips from radium. C. F. L. has punctate keratoses and dry finger pads of thumb, index and middle fingers, worse on the left hand. These areas represent sites of closest contact with needles, when tissue was stretched or held when inserting needles. Early in his career, needles with steel alloy walls, which did not filter as well as the present ones, were used. It is felt that the effects on his fingers are due chiefly to beta rays, since there are not the bone changes (rarefaction) that one would expect if the changes were due to the more homogeneous and penetrating gamma radiation. Again, C. F. L. did not use lead finger tips early in his carreer, as both he and J. L. P. do now when in close proximity to radium (fig. 3 *G*).

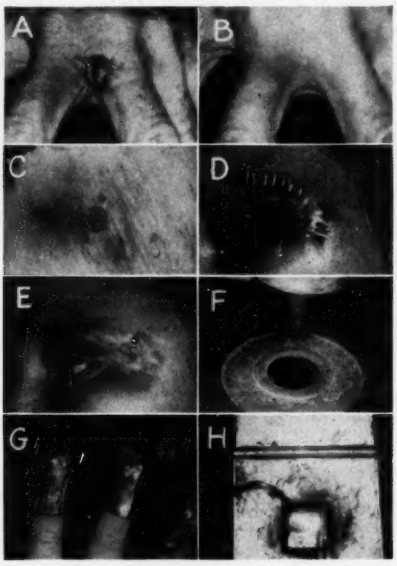

Fig. 3.—*A*, triangle arrangement in keratoma. *B*, result after two months. *C*, arrangement of needles in basal cell cancer. Distance between needles, 5 mm. *D*, advanced basal cell cancer, duration three years. *E*, result after four months. *F*, radium well—4 inches (10 cm.) lead thickness. *G*, lead finger cots. *H*, lead carrying case for radium, pick-up and insertion forceps.

Patients having radium on them are placed in a room behind a wall that is lined with 3 mm. of lead. This room is at one end of the office, and the operators do not get near it except to insert or remove the radium. When not in use, the radium is kept in a lead capsule of 4 inch (10 cm.) wall thickness (fig. 3 *F*).

By use of the Victoreen minometer the amount of radiation absorbed by physicians and technicians has been recorded at various times. The amount of radium (in needles) handled during a full day by three physicians and three assistants varies from 0 to 150 mg. Measurements with the Victoreen minometer of radiation absorbed have been from 0.07 on an average up to 0.2 roentgen. The latter amount is reached rarely, i. e., when one person handles all the radium as much as twice per day.

Blood counts are made on personnel at six month to yearly intervals, and to date none of us has had leukemia.

Another disadvantage of this technic might be stated to be the investment in a considerable amount of radium. With present day cost of radium the outlay is not very great. One could do considerable work with only six 10 mg. needles, and would find this technic quite handy if one were in a location where skin cancer is prevalent. The cost of construction of an office and of lining the walls with lead would be much more than the cost of the radium.

COMMENT

From January 1931 to August 1949, 5,490 lesions were treated with the short intensive technic, as follows:

Face (temple, forehead, cheeks)	1,737
Nose	1,124
Lower lip	796
Ear	519
Canthus and eyelid	317
Neck	273
Lips (precancerous lesions)	158
Upper lip	135
Chin	94
Miscellaneous (i. e. back, finger, etc.)	337

During this time there were 123 lesions treated with the long, low intensity technic.

We cite these figures to show that we would select other methods of interstitial radiation when we felt that it was more advantageous to do so. Our statistics on cure rate are not yet ready for a very critical analysis and will not be presented here. Since we have had numerous requests for a description of the short technic we decided to publish it first and allow more time to assemble statistics more accurately than we now have. Therefore from the statistical viewpoint this paper will not be convincing. Nevertheless, we are confident that if used with judgment, this method is a very valuable adjunct to therapy of small superficial skin cancers when good cosmetic results and the short time factor are desired.

ABSTRACT OF DISCUSSION

Dr. George C. Andrews, New York: I wish to compliment Drs. Lehmann and Pipkin on the carefully prepared summary of their experience during the last 20 years with interstitial radium therapy. Their paper leaves no doubt that they completely understand and are masters of their subject. They have mentioned the disadvantages as well as the advantages of their technic, which uses needles containing 10 mg. of radium and having a wall thickness of 0.3 mm. of platinum. This can be contrasted with the use of small needles containing 0.6 mg. by Drs. Everett Fox, Jesse Shelmire and Charles Martin, all of the neighboring city of Dallas. The Janeway Lecture given before the American Radium Society in June 1949 by Dr. Martin was a most convincing exposition of the use of low intensity needles, and I notice that the present authors have been modest enough in their paper to state that in certain infiltrating ulcerative cancers with deep induration the use of low intensity needles is preferable.

I believe that most radiologists will agree on these points and that mathematical determination of the tumor dose in gamma roentgens by the Paterson and Parker and the Quimby tables is extremely desirable. However, the personal training and individual skill of these various men of wide experience is, generally speaking, of greater importance than the differences in the technics which they use.

In cancer of the lids and about the eyes I believe that one is able to protect the eyeball better if one uses low voltage roentgen rays, especially contact therapy. This point is, of course, debatable.

It interests me that Drs. Lehmann and Pipkin do not countersink the needles so that the ends are entirely embedded, as is customary in the use of small low intensity needles. Perhaps the two or three hours that their needles are inserted is so short a time that they do not become displaced. This is contrasted to the seven day period used for the small low intensity needles. I should like to ask about this point. In closing, I should like to congratulate the authors on a very excellent and interesting paper.

DR. JOHN H. LAMB, Oklahoma City: I think Drs. Lehmann and Pipkin are to be congratulated as pioneers in the field of radium therapy. Here again they have brought out a new technic for the treatment of malignant skin growths with a saving of the patient's time. However, this is not as important as adequate protection of the nurses and physicians from the effects of radiation.

The Committee on Physics of the National X-Ray Societies has recommended that the human can stand a daily tolerance dose of 0.1 r per day. There is now available a new portable pencil roentgen meter, called a minometer and produced by the Victoreen Company, the chamber of which measures up to 0.2 r. I recommend that all of those doing radiation therapy avail themselves of this safeguard for both themselves and their staffs. In one morning's insertion of the weak interstitial needles (1 mg. per running centimeter of tissue) in three or four consecutive cases, we are exposed only to an average of 0.02 or 0.03 of radiation, which observation proved to us the safety of the operation of this means of radiation. If this short intense technic will give as minimal an exposure to the operators, then I am for a trial of this method of treatment. If the operators are changed each day and have to work only every third day, then a much greater exposure is permissible.

DR. C. F. LEHMANN, San Antonio, Texas: Regarding Dr. Andrews' question as to whether or not we sew in these 10 mg. needles, we do not. We feel that adhesive tape holds them in place well enough for this short length of time. We do sew in the needles of low intensity that are left in place one week, using a fine wire that fixes them and holds them very well. We feel that the method of interstitial radiation is far superior to the use of roentgen rays and is far superior to the use of radon because we know the dose is going to stay where it is put. We have no argument at all with other methods of treatment. We believe that unless one uses radiation of too soft quality, delivered by means of contact x-ray apparatus, the scars are practically identical. We have seen a lot of bad scars as a result of some of the older methods of using roentgen rays, scars that will not hold up. This possibility is an important consideration.

For instance, in the treatment of the morpheic type I believe there is an illustration of this general law of radiation. Whenever one uses radiation one should think of the after-result, of whether the scar is going to heal and hold up. When one applies treatment to cancer I think one should always use the axiom of endeavoring, not for what is going to cure the patient, necessarily, but for what is going to give him the least disadvantages later on. That aim should get more consideration in all cancer therapy.

I think Dr. Lamb's advice and admonition are very appropriate. We stagger our workers in using radium, with three physicians doing it. The only time anyone gets an overdose is when the other two are playing hooky or away; we also stagger the time of radium handled by our technicians. We always try to protect the nurses by giving them sufficient time off. I believe that, as a safety limit, 0.2 should be set as the daily tolerance; and Dr. Lamb says the amount should be 0.1 r.

DR. JOHN H. LAMB, Oklahoma City: I still think 0.1 r should not be exceeded as the daily tolerance dose.

EARLY PROGNOSIS OF LUPUS ERYTHEMATOSUS DISCOIDES

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LUPUS erythematosus discoides is a chronic inflammatory dermatosis, and the remedies which have been used in its treatment are legion. Nevertheless, the results of treatment are still unsatisfactory. Sequeira, Ingram and Brain [1] state that 30 per cent of the patients are cured, 30 per cent improved and 40 per cent unchanged after treatment. Sutton and Sutton,[2] discussing the prognosis of the disease, state that this should always be guarded and that the disease is erratic in its course, with occasional recurrences and relapses common. They also state that new patches sometimes develop and older ones extend despite the employment of approved therapeutic measures.

No one has yet been able to forecast, however, which cases will and which cases will not react to treatment. I will describe in this article a simple method of obtaining an early and reliable prognosis in cases of this capricious disease. It will also be shown that this method can give information as to the state of activity of the lesions and their subsequent progress during and after treatment. This last point is important, as it may help in the prevention of relapses and recurrences common to the disease.

This method, now to be described, is the careful study of erythrocyte sedimentation rates in lupus erythematosus discoides.

Although the performance of erythrocyte sedimentation rate determinations is frequently done in sanatoriums and during the treatment of rheumatism and allied disorders to judge the progress of a case, little use of this simple test seems to have been made in dermatology. Tulipan and Director [3] used the readings of erythrocyte sedimentation rates as aids in the differential diagnosis of allied skin diseases. I, however, used them, not in this manner, but to obtain the information mentioned above.

Eighty-three cases of lupus erythematosus discoides were investigated by this method. Sixty were in females and 23 in males. The ages of the patients varied from 12 to 63 years, and the disease had been present from two weeks to 20 years.

The Westergren method was used in each case, and the erythrocyte sedimentation rate was estimated at two attendances before treatment commenced and then

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This work was done during tenure of a McIntyre Clinical Research Scholarship in Dermatology.

1. Sequeira, J. H.; Ingram, J. T., and Brain, R. T.: Diseases of the Skin, ed. 5, London, J. & A. Churchill, Ltd., 1947, p. 254.

2. Sutton, R. L., and Sutton, R. L., Jr.: Diseases of the Skin, ed. 10, London, Henry Kimpton, 1939, p. 368.

3. Tulipan, L., and Director, W.: Red Cell Sedimentation Test in Dermatology, Arch. Dermat. & Syph. **27**:759 (May) 1933.

again on two or more occasions eight weeks after the start of treatment. If the patient was showing improvement under treatment the sedimentation rate was finally estimated at the end of treatment. No tests were done during menstruation or if the patient appeared to be suffering from any complicating disease, such as the common cold, at the time. Variable factors such as room temperatures and air currents were controlled as carefully as possible. Westergren [4] was of the opinion that an erythrocyte sedimentation rate of 1 to 3 mm. at the end of one hour was normal in the male and one of 4 to 7 mm. normal in the female. Other authorities, however, have thought the normal to be considerably higher, and so for these tests any reading below 10 mm. in the first hour was regarded as within normal limits. Between 10 and 30 mm. was considered abnormal, and over 30 mm., very decidedly pathological.

In addition to the erythrocyte sedimentation rate determinations in the 83 cases of lupus erythematosus discoides, similar investigations were carried out in 80 cases of miscellaneous dermatoses as a control series. This control series consisted of 10

TABLE 1.—*Erythrocyte Sedimentation Rates in Lupus Erythematosus Discoides and Various Other Diseases*

Lupus Erythematosus Discoides				Controls				
	A	B	C			A	B	C
No. of Cases	(1-10 Mm. in 1 Hr.)	(10-30 Mm. in 1 Hr.)	(30 Mm. or More in 1 Hr.)	Diagnosis	No. of Cases	(1-10 Mm. in 1 Hr.)	(10-30 Mm. in 1 Hr.)	(30 Mm. or more in 1 Hr.)
..	..	..	..	Eczema	20	15	5	..
..	..	..	..	Psoriasis	10	9	1	..
..	..	..	..	Dermatitis herpetiformis	10	8	2	..
..	..	..	..	Acne vulgaris	15	11	4	..
..	..	..	..	Urticaria	10	8	2	..
..	..	..	..	Alopecia areata	6	4	2	..
..	..	..	..	Lichen planus	5	4	1	..
..	..	..	..	Granuloma annulare	4	4	0	..
83	17	57	9	Total	80	63	17	..

cases of psoriasis, 10 cases of urticaria, 10 cases of dermatitis herpetiformis, 15 cases of acne vulgaris, 20 cases of sensitization eczema, 6 cases of alopecia areata, 5 cases of lichen planus and 4 cases of granuloma annulare. The results of the determinations in the cases of lupus erythematosus discoides and the control series are recorded in table 1.

From table 1 it is seen that in lupus erythematosus discoides no less than 57 (68.6 per cent) cases had abnormal results and a further 9 (10.8 per cent) cases had very decidedly pathological ones. A total of 66 (79.4 per cent) cases gave a result which was above normal. In the control series, on the other hand, no less than 63 (78.7 per cent) cases presented figures which had to be accepted as within normal limits. It would appear therefore that the erythrocyte sedimentation rate has a definite relationship to the lesions of lupus erythematosus discoides, and it now remains to be seen whether information can be obtained from this observation which may lead to a method of establishing an early prognosis of the disease.

The erythrocyte sedimentation rates are divided into three groups, A, B and C, as shown in table 1. The lesions of lupus erythematosus discoides are differen-

4. Westergren, A.: The Technic of the Red Cell Sedimentation Reaction, Am. Rev. Tuberc. **14**:94 (July) 1926.

tiated by the author into two distinct varieties: (1) seborrheic-like lesions, dull, erythematous, infiltrated patches of indolent appearance with raised and apparently inactive nonspreading edges, the centers of the lesions being irregular, depressed and covered with thick yellowish gray or white adherent scales, and (2) erythematous lesions, bright erythematous areas of active appearance, the borders of which are well defined and which, although slight induration may be present, have no thickening or raising of the edges, while the centers are smooth and shining and widely dilated follicles are a prominent feature, usually with no or slight scaling.

Group A consisted of 17 patients, five of whom had lesions of the seborrheic type and 12 of whom had the erythematous type.

Group B consisted of 57 patients, 24 of whom had seborrheic lesions and 30 of whom had erythematous lesions. Two of the remaining three patients had the rare telangiectatic lesions while the third patient had a deep-seated nodular type of lesion.

Group C included nine patients, four of whom had the seborrheic type of lesion and 5 of whom had the erythematous type.

TABLE 2.—*Results of Treatment in Cases of Lupus Erythematosus Discoides*

Clinical type of lesion	Group A		Group B		Group C	
	Erythematous	Seborrheic	Erythematous	Seborrheic	Erythematous	Seborrheic
Total	12	5	33	24	5	4
No. cured	9	..	16	16	..	..
No. decidedly improved	3	..	12	3	1	1
No. of treatment failures	..	5	5	5	4	3

Treatment of these 83 patients was carried out with sulfatriad® (sulfadiazine, 37.5 per cent; sulfathiazole, 37.5 per cent, and sulfamerazine, 25 per cent) and oxophenarsine hydrochloride (Mapharside). The method of treatment chosen was determined by various causative and clinical factors investigated by the author. Sulfatriad® was the drug used in cases in which there was evidence of focal infection. Oxophenarsine hydrochloride was used in cases with a tuberculous connection, as in a previous series of published cases I [5] had shown this drug to be of use in this type of case. The results of treatment in the various groups are summarized in table 2.

COMMENT

In group A the five patients with the seborrheic lesions did not respond to treatment and could be classed as showing failure of treatment. Of the 12 patients with erythematous type lesions nine were clinically cured and three were decidedly improved. The results suggest that the prognosis is poor in cases clinically chronic in appearance and combined with a low erythrocyte sedimentation rate indicating that the disease is only slightly active. With the erythematous type of lesion, however, a low grade of activity as shown by a low erythrocyte sedimentation rate seems to indicate an excellent prognosis.

5. Cochrane, T.: Mapharside Treatment of 56 Cases of Lupus Erythematosus Discoides, Glasgow M. J. **30**:222 (June) 1949.

In group B, 19 of the 24 cases with seborrheic lesions gave a good response to treatment and only five cases could be considered as showing treatment failures. As stated previously with regard to group A, the clinically chronic appearance of this type of lesion, if considered by itself, does not indicate a good prognosis. When the erythrocyte sedimentation rate is considered, however, it is observed that this test indicates a moderate degree of activity in the diseased areas. It appears indicated that in patients such as these 24 with seborrheic type lesions and sedimentation rate moderately raised the prognosis is good in spite of the clinically chronic appearance of the lesions and that treatment offers reasonable chances for recovery. Of the 30 patients with erythematous type lesions all but five responded satisfactorily to treatment. Thirteen persons were clinically cured and 12 decidedly improved. Of the three patients with unusual forms of the disease, all could be classed as clinically cured after treatment. If the cases with erythematous lesions in group B are compared with the cases with erythematous lesions in group A, the percentage of clinical cures in group B is seen to be less. It would seem, therefore, that with the erythematous type of lesion the erythrocyte sedimentation rate, although not so definite a guide to prognosis as in the seborrheic variety of the disease, does indicate nevertheless the chance of cure. The lower the erythrocyte sedimentation rate, the better the chance of cure in the cases with erythematous lesions.

In group C all nine patients had numerous and widespread lesions and even the cases with seborrheic lesions showed evidence of intense activity indicated by bright erythematous and more than normally infiltrated thickened borders. A satisfactory result was obtained in only two cases, in both of which the erythrocyte sedimentation rate was 32 mm. in the first hour. It would seem, therefore, that in cases of lupus erythematosus discoides with a sedimentation rate of more than 35 mm. in the first hour, no matter what the variety of the clinical lesion, a poor prognosis is indicated and response to treatment is unsatisfactory.

There seems, therefore, to be sufficient evidence to show that in lupus erythematosus discoides determination of the erythrocyte sedimentation rate is a reliable and yet simple test as to the state of activity of the lesions and provides an early indication of their prognosis and response to treatment. Roxburgh and Corsi [6] and Strandberg [7] noted in their respective series of cases of lupus erythematosus discoides that the shorter the duration of the disease, the better was the chance of cure with treatment. I, however, consider that the combination of clinical lesion and erythrocyte sedimentation rate provides a much more reliable guide to the prognosis of the disease. This statement appears to be substantiated by the fact that in 14 of the 22 cases which did not respond to treatment the disease had been present for three years or less and so accordingly the prognosis should have been good. By the erythrocyte sedimentation rate, however, no less than nine of these 14 unsatisfactory cases had a poor prognosis and two only had a fair prognosis.

The effect of treatment on the erythrocyte sedimentation rate was observed by performing this test as described previously after the eighth week and again at the end of the course of treatment. It was obvious from these observations that as lesions improved the rates gradually decreased and, finally, of the 61 patients who

6. Roxburgh, A. C., and Corsi, H.: The Therapeutic Value of Gold Compounds (Sanocrysin, Krysolgan, etc.), Brit. J. Dermat. **42**:382 (Aug.) 1930.

7. Strandberg, J.: Six Years' Experience of Treatment of Lupus Erythematosus with Gold Compounds, Acta med. Scandinav. **75**:296, 1931.

could be classed as having satisfactory responses to treatment, only eight had an erythrocyte sedimentation rate of over 10 mm. in one hour, whereas before treatment no less than 49 of these patients had abnormally high sedimentation rates. In these eight patients, the final rate was never greater than 13 mm. in the first hour and was always much lower than the original rate. During the subsequent 24 months after cessation of treatment, each of the 61 cases with satisfactory outcome was reviewed every two or three months and a sedimentation rate determination was performed. During this period, five patients relapsed, three of whom had been treated with sulfatriad and two of whom had received oxophenarsine hydrochloride.

In two cases relapse of the lesions occurred within five months of the end of treatment, while in the other three cases recurrence of the disease took place between six and eight months after cessation of treatment.

It is interesting to note that in four of the five cases there was a rise in the erythrocyte sedimentation rate of more than 8 mm. in one hour while in the fifth case only a rise of 3 mm. was obtained. A further interesting factor was that four of the five cases with relapse belonged to the group of eight cases that showed a final rate of 10 mm. or over subsequent to treatment. A sedimentation rate determination performed at monthly intervals for a year might therefore give warning of a possible relapse and allow early treatment to be started and thus minimize the danger of this occurrence. Special attention should be paid to successfully treated cases in which there was, however, a final erythrocyte sedimentation rate of 10 mm. or over.

SUMMARY

Erythrocyte sedimentation rate determinations have been performed in 83 cases of lupus erythematosus discoides and treatment carried out.

It has been shown that this simple test can be used as a reliable guide to the state of activity of the lesions.

When correlated with the clinical appearances of the lesions, the erythrocyte sedimentation rate can give an early indication of the prognosis of the disease.

In satisfactorily treated cases, this test may be used as a means of detecting, treating and perhaps minimizing an early relapse of the lesions of lupus erythematosus discoides.

NEUTROPHILS RESEMBLING L. E. CELLS IN ARTIFICIAL BLISTERS

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AND
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THIS IS a report of studies of the cellular elements in the fluid obtained from artificial blisters produced on the skin of patients with acute disseminated lupus erythematosus.

From the reports of others [1] it would seem that L. E. cells may be formed in a patient with acute disseminated lupus erythematosus whenever plasma from such patients and neutrophilic leukocytes are placed together under favorable conditions. Unaltered plasma may not be obtained in blister fluid because the dermis may filter out some of its components. However, most of the blister fluid is filtered plasma. As neutrophilic leukocytes are present in blister fluid, it was thought that L. E. cells might also be present in blister fluid from patients with acute disseminated lupus erythematosus. As natural blisters are formed only rarely in disseminated lupus erythematosus, artificial blisters were produced with cantharides on patients wih lupus erythematosus, as well as on those with various other diseases, and a study was made of the cell types found in the blister fluid.

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Abridgment of paper submitted by Dr. Watson to the Faculty of the Graduate School of the University of Minnesota in partial fulfilment of the requirements for the degree of Master of Science in Dermatology and Syphilology.

1. (*a*) Morton, R. J.: A Study of the Blood and Bone Marrow in Cases of Disseminated Lupus Erythematosus, Thesis, University of Minnesota Graduate School, 1947. (*b*) Hargraves, M. M.; Richmond, H., and Morton, R. J.: Presentation of 2 Bone Marrow Elements: The "Tart" Cell and the "L. E." Cell, Proc. Staff Meet., Mayo Clin. **23**:25-28 (Jan. 21) 1948. (*c*) Haserick, J. R., and Sundberg, R. D.: The Bone Marrow as a Diagnostic Aid in Acute Disseminated Lupus Erythematosus: Report on the Hargraves' "L. E." Cell, J. Invest. Dermat. **11**:209-213 (Sept.) 1948. (*d*) Sundberg, R. D., and Lick, N. B.: "L. E." Cells in Blood in Acute Disseminated Lupus Erythematosus, ibid. **12**:83-84 (Feb.) 1949. (*e*) Hargraves, M. M.: Production in Vitro of the L. E. Cell Phenomenon: Use of Normal Bone Marrow Elements and Blood Plasma from Patients with Acute Disseminated Lupus Erythematosus, Proc. Staff Meet., Mayo Clin. **24**:234-237 (April 27) 1949. (*f*) Haserick, J. R., and Bortz, D. W.: Normal Bone Marrow Inclusion Phenomena Induced by Lupus Erythematosus Plasma, J. Invest. Dermat. **13**:47-49 (Aug.) 1949. (*g*) Haserick, J. R.: Blood Factor in Acute Disseminated Lupus Erythematosus, Arch. Dermat. & Syph. **61**:889-891 (June) 1950. (*h*) Gueft, B.: Depolymerization of Nucleic Acid in Acute Disseminated Lupus Erythematosus, ibid. **61**:892-897 (June) 1950.

TECHNIC

The material used to produce the artificial blister is cantharides cerate N. F. (fig. 1). A small amount of this paste is placed on the center of an adhesive patch such as is commonly used by dermatologists for patch testing. The paste is easily placed on the adhesive patch with a wooden applicator, with the formation of a flat, circular mass from 0.5 to 1.0 cm. in diameter. A diameter of 0.5 cm. usually will make a blister large enough to furnish adequate fluid when only direct smears of the blister fluid are made. Formation of a cantharides blister only 0.5 cm. in diameter is associated with very little, if any, discomfort to the patient.

The site selected for application of the patch was an area of normal skin on the anterior surface of the lower portion of the thigh (fig. 2*a*). This area has two main advantages. The

Fig. 1.—Equipment used in producing a cantharides blister and in making smears of cantharides blister fluid.

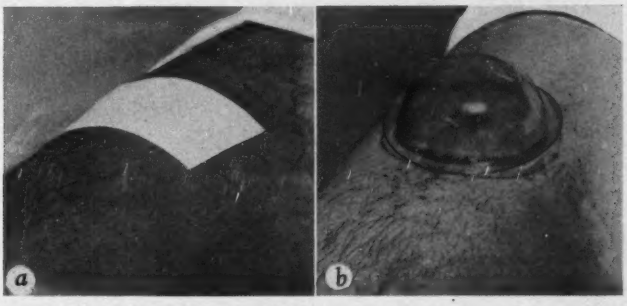

Fig. 2.—(*a*) Cantharides patch on right thigh. (*b*) Plastic cup covering cantharides blister.

blister is not easily broken during sleep unless the patient sleeps prone. Patients do not object to this test site for cosmetic reasons because it is ordinarily well concealed from view.

The area is shaved so that the paste will have better contact with the skin. Also, hairs hinder the formation of a cantharides blister. An alcohol sponge is used to cleanse the area before application of the patch.

The patch is left in place for three or 3½ hours. After the patch has been removed, the area is gently cleansed with an alcohol sponge to remove any of the paste that remains. Most of the paste sticks to the patch so that very little paste remains on the skin to be removed with the alcohol sponge.

A small transparent plastic cup is used to protect the area where the blister is formed (fig. 2*b*). The cup is held loosely in place by means of two or more strips of scotch® tape or adhesive plaster. The cup prevents rupture of the blister, and it also permits observation of its growth without removal of the protective covering.

About 24 hours after the cantharides patch has been applied, the blister is uncovered (fig. 3) and direct smears of the blister fluid are made. If a blister did not form on first application, the procedure is repeated, except that with this second attempt the patch is allowed to remain on the skin for four hours.

After the blister is gently cleansed with an alcohol sponge, the roof is cut open with a small, sharp-pointed scissors. The opening is made large enough so that a small dermal curet can be introduced into the opening. The curet is gently moved around inside the blister, thus mixing the fluid and slightly curetting the base so that a well mixed sample is obtained.

The drop of blister fluid on the curet is then smeared on two glass slides. It is important that the smears be dried immediately by being waved briskly in the air, because we have found that the cellular detail is much clearer in preparations which are dried rapidly in this manner.

Any number of smears can be made, how many depending on the number of slides desired or the amount of blister fluid present. Four good smears are adequate to demonstrate the cellular detail present and to insure against incidental accidents to the slides.

After the smears have been made, the area of the blister is covered with a small gauze bandage. There is no scarring as a result of the blister. Slight pigmentation remains for one or two months, after which no sign of injury to the area can be detected.

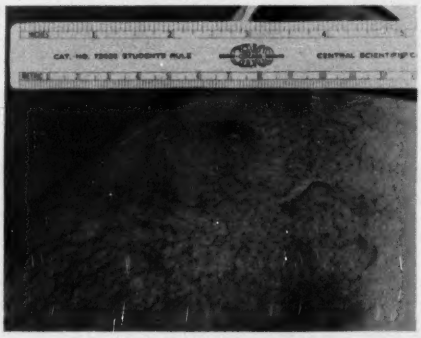

Fig. 3.—Cantharides blister formed on the thigh of one of the authors. A patch had been placed on this area 24 hours previously. Pain or discomfort was not associated with formation or subsequent resolution of the blister.

The smears are stained with Wright's stain for a minute and a half, after which a buffer is added. The buffer is made up as follows: 6.63 Gm. of monobasic potassium phosphate, 2.56 Gm. of dibasic (anhydrous) sodium phosphate, 1,000 cc. of distilled water and 4 drops of chloroform (for a preservative). It should be at p_H of 6.4. The stain and buffer are left in place for five minutes. Then the slides are washed with distilled water and dried.

There are advantages to using a small dermal curet in obtaining and smearing the blister fluid. Some of the cells have a higher specific gravity than the fluid and therefore may be lying on the floor of the blister. However, when the fluid is smeared with another glass slide, as is done in making blood smears, the heavier cellular elements are more commonly seen in the end or outer portions of the smear. Thus a droplet of fluid obtained by aspirating the blister may not contain the heavier cellular elements. In aspiration of the fluid with a needle and syringe a clot forms in the syringe in three to four minutes, preventing its further use. If heparin or potassium oxalate is used in the syringe to prevent clotting certain disadvantages may be noted. If the concentration of heparin is too strong the cells will appear "burned" and may disintegrate rapidly; also amorphous material appears on the slide, making a poor preparation. When potassium oxalate is used, the polymorphonuclear leukocytes may ingest the oxalate crystals and obscure cellular detail. If the fluid is to be drawn into a syringe

and later centrifuged, more blister fluid is needed, and hence a large blister must be produced. Oxalation, heparinization and centrifugation, either alone or in combinations, were used earlier in this study, but these procedures were eliminated for the reasons indicated above.

PECULIAR NEUTROPHILIC LEUKOCYTE

The peculiar neutrophilic leukocyte (fig. 4 *a* to *d*) is found in direct smears of fluid from artificial blisters obtained only from patients having acute disseminated lupus erythematosus. This cell contains one or several inclusion bodies. The color of these bodies, when stained with Wright's stain, is usually robin's egg blue. Occasionally the color is darker and may have a greenish tint. The bodies are globular and vary in size. Usually the bodies are discrete, but occasionally they seem to be coalescing, and there may be as many as 10 or 15 bodies in a single neutrophilic leukocyte. The nucleus of the cell is occasionally degenerating.

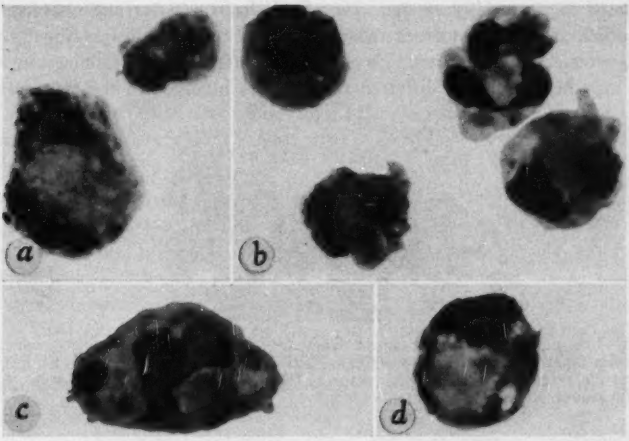

Fig. 4.—Smears of fluid from cantharides blisters made in cases of acute disseminated lupus erythematosus. (*a*) The larger cell is a peculiar neutrophilic leukocyte. In its center is a large, single, bluish body. The smaller cell is a normal neutrophilic leukocyte (× 1,700). (*b*) The cell farthest to the right is a peculiar neutrophilic leukocyte. It contains a bluish body which is slightly smaller than the bluish body in *a* of this figure. The other three neutrophilic leukocytes show some signs of degeneration, but otherwise they are normal (× 1,700). (*c*) This peculiar neutrophilic leukocyte contains more than 15 bluish bodies of various sizes. Most of the bluish bodies are discrete, but some of them appear to be coalescing (× 1,700). (*d*) The bluish body in this peculiar neutrophilic leukocyte appears to have been formed by coalescence of three or more smaller bluish bodies (× 1,700).

This peculiar neutrophilic leukocyte was found in cantharides blister fluids from 5 patients with acute disseminated lupus erythematosus. The cell was not found in blister fluid from eight normal persons or in that from six patients with chronic discoid lupus erythematosus. Smears of cantharides blister fluid from patients having other diseases did not contain the peculiar neutrophilic leukocyte. In the control group studied were three persons with dermatomyositis, two with rheumatoid arthritis and one each with acute rheumatic fever and scleroderma. Studies of artificial blister fluid were also negative for this

characteristic cell in six cases of pemphigus, four cases of dermatitis herpetiformis, two cases of erythema multiforme, nine cases of atopic dermatitis, seven cases of eczematoid dermatitis, five cases of psoriasis, two cases of mycosis fungoides and one case each of myelogenous leukemia, lichen planus and dyshidrotic eczema.

The number of these peculiar neutrophilic leukocytes found in direct smears of cantharides blister fluid is usually smaller than the number of L. E. cells found in smears from material obtained on sternal aspiration.

A few mononuclear cells, which are possibly histiocytes, also contain a similar bluish body. However, this phenomenon is seen in other diseases as well as in acute disseminated lupus erythematosus.

COMMENT

One of us (M. M. H.) studied these cells obtained in the five cases of acute disseminated lupus erythematosus. He noted that the color and character of the bluish bodies are different from those of the inclusion bodies in the L. E. cells obtained on sternal aspiration. He suggested that these differences in staining reaction may be due to the different time factors involved in the two procedures.

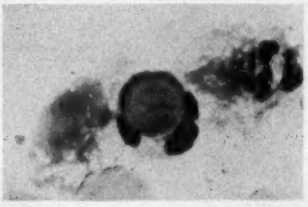

Fig. 5.—"L. E." cell in smear made from freshly aspirated heparinized bone marrow material from a patient with acute disseminated lupus erythematosus. It shows nuclear material in a digestive vacuole of a bilobed neutrophilic polymorphonuclear leukocyte (× 900). (From Hargraves, Richmond and Morton.[1b])

It is interesting to note that the neutrophilic leukocytes seen in centrifuged, oxalated blister fluid resemble more closely the L. E. cells obtained on sternal aspiration (fig. 5) than they do those found in direct smears of blister fluid.

In a sense, the cantharides blister is an in vitro method of incubating plasma and various cells. That fact may explain why direct smears of the cantharides blister fluid contain the peculiar neutrophilic leukocyte while direct smears of bone marrow do not have L. E. cells. It is a known fact that the L. E. cells are found in bone marrow only after several minutes have elapsed between the time of obtaining the marrow and making the smear. Likewise, when L. E. cells are found in peripheral blood, as described by Sundberg and Lick,[1d] several minutes must elapse between the time of drawing the blood and making the smear.

When the L. E. cell is demonstrated in the bone marrow or peripheral blood, the specimen contains an anticoagulant and the number of such cells is increased by centrifugation. Anticoagulants and centrifugation are not needed to demonstrate the peculiar neutrophilic leukocyte in artificial blister fluid.

Small cantharides blisters may be formed on a patient in order to determine the severity of the disease as it waxes and wanes, as these cells decrease in number

or disappear entirely as the patient has a remission. No more than three artificial blisters were formed on any one patient of the group that made up the basis of this report.

Further studies will have to be made in order to explain the origin and significance of the bluish bodies found in the peculiar neutrophilic leukocyte. Perhaps these bodies are of a different nature from those found in neutrophilic leukocytes in bone marrow preparations. Since the etiology and pathogenesis of acute disseminated lupus erythematosus are still obscure, the significance of these peculiar neutrophilic leukocytes remains uncertain.

SUMMARY

A differential smear of cantharides blister fluid in five cases of acute disseminated lupus erythematosus contained a peculiar neutrophilic leukocyte. This cell contains one or several bluish bodies and resembles an L. E. cell such as is found in material obtained on sternal aspiration from patients with acute disseminated lupus erythematosus. This peculiar neutrophilic leukocyte was not seen in smears of cantharides blister fluid from normal persons or in that from patients with other diseases.

The study of artificial blister fluid from patients with acute disseminated lupus erythematosus seems to offer a new approach to that disease. It may be of diagnostic value.

ADDENDUM.—After submission of this article for publication, cantharides blisters were produced and aspiration of sternal marrow was done in 12 additional cases of acute and subacute disseminated lupus erythematosus. The peculiar neutrophilic leukocyte was found in direct smears of fluid from cantharides blisters in each case. However, the L. E. cell was found in special preparations of sternal marrow in only nine cases. Thus, in three cases the artificial blister test seemed to be a more sensitive indicator of subacute disseminated lupus erythematosus than was examination of aspirated material from sternal marrow.

DERMATITIS AND SECONDARY LEUKODERMA DUE TO FABRIC-LINED RUBBER GLOVES

Report of a Case

I. BOTVINICK, M.D.
DETROIT

DERMATITIS due to use of synthetic rubber gloves is infrequent. For patients with so-called "housewife's" eczema of the hands, dermatologists frequently recommend the use of cotton or fabric-lined rubber gloves for household chores. A recent experience suggests that this recommendation carries with it added risks as well as safeguards, and the following case is reported to emphasize the risk.

REPORT OF CASE

G. T., a 40 year old white housewife, was seen on Sept. 27, 1949, complaining of an extremely pruritic dermatitis of the forearms and wrists of 10 days' duration. Examination revealed a patchy, erythematous, edematous, vesicular dermatitis of the lower two thirds of the flexor aspects of both forearms, the wrists and the dorsal surfaces of several fingers of both hands. Since the distribution of the eruption was suggestive of a contact dermatitis, the patient was questioned in detail regarding possible contact factors. It was learned that the patient had used bluettes® gloves (Pioneer Rubber Company, Willard, Ohio) in her household tasks for approximately two months prior to the onset of the dermatitis.

Patch tests were performed with portions of smooth blue rubber of the outer surface and the rubberized fabric of the inner surface of the bluettes.® Both samples were applied to the anteromedial surface of the left arm and were removed in 40 hours. The test sites were slightly elevated, erythematous and studded with superficial vesicles. Five days after the patch tests were removed the sites were even more decidedly elevated and edematous and the vesicles were larger.

The patient remained under observation and treatment until Oct. 17, 1949. Treatment consisted in the following local applications: compresses of aluminum acetate (Burow's) solution in 1 to 20 dilution; 0.25 per cent menthol, 1 per cent phenol and 2 per cent camphor in aquaphor® (an oxycholesterol-petrolatum ointment base); 2 per cent salicylic acid in white petrolatum, and zinc oxide ointment. Diphenhydramine hydrochloride was administered intravenously and orally. An elixir of chloral hydrate and sodium bromide was administered for mild sedation. Superficial roentgen radiation, in doses of 75 r, was administered on three occasions. A single suberythema dose of ultraviolet radiation was given. The dermatitis responded slowly to treatment until Oct. 11, 1949. On that date the patient wore white cotton gloves under golden glo® household gloves (Faultless Rubber Company, Ashland, Ohio) in washing dishes and clothes. The next day a flare-up of the dermatitis and a recurrence of severe pruritus were noted.

From Oct. 18 to Oct. 26, 1949, the patient was hospitalized at the University Hospital, Ann Arbor, Mich. On admission dryness and superficial scaling of the hands were evident. Blotchy areas of erythema had appeared on the face a few hours before the patient's admission to the hospital.

The patient's hospital course was stormy. On the second day she manifested a generalized pruritic, erythematous, urticarial rash and became extremely disturbed emotionally, to the point of requiring restraints.

The patient was treated for varying periods with oral diphenhydramine hydrochloride, doxylamine (decapryn®) succinate, chloral hydrate, codeine, meperidine (demerol®) hydrochloride, colloidal and coal tar solution baths, wet dressings with aluminum acetate solution in 1 to 15 dilution, 1 per cent salicylic acid in petrolatum and one fever treatment with intravenously administered typhoid vaccine.

At the time of the patient's discharge the generalized urticarial rash had faded completely and the arms and hands showed signs of healing. It was the impression of the staff that the patient had a contact dermatitis and dermatitis medicamentosa and that diphenhydramine hydrochloride was responsible for the emotioinal disturbance.[1]

I saw the patient again on Dec. 8, 1949. The skin of both wrists and forearms was dry. There were scattered areas of leukoderma at the sites where the dermatitis had been most severe and persistent. There was also an area of leukoderma at the sites where the patch tests had been applied. The patient refused to permit further patch test studies.

On June 16, 1950 the patient returned for examination. Repigmentation was noticeable, particularly around follicular orifices, with resultant speckling of the leukodermic areas. Since Age Rite Alba,® or monobenzyl ether of hydroquinone, is the only compound used in the manufacture of rubber articles which has been reported to produce transitory leukoderma,[2] it was suspected that the leukoderma exhibited by this patient was due to that agent.

Information regarding the manufacture and the processing of the bluettes® was requested from the Pioneer Rubber Company. The only information obtained was that the gloves were made from Du Pont neoprene and that calcium chloride was used in coagulation of the neoprene latex. No information about the use of monobenzyl ether of hydroquinone could be obtained. Tests for detection of Age Rite Alba in one of the bluettes® gloves were done by a private laboratory. Age Rite Alba was present in the glove. The Faultless Rubber Company stated that golden glo® household gloves are made with natural rubber latex. Additional information was not given.

SUMMARY

The history of a white woman who acquired a severe contact dermatitis followed by transitory leukoderma after the use of bluettes® gloves is reported. The dermatitis and leukoderma were reproduced by patch tests with material from the gloves. Laboratory tests revealed the presence of Age Rite Alba, or monobenzyl ether of hydroquinine in one of the bluettes® gloves. The dermatitis was aggravated by contact with natural latex rubber gloves.

610 Maccabees Building (2).

1. Abstract of a case summary obtained from Dr. Udo J. Wile.

2. Schwartz, L.; Oliver, E. A., and Warren, L. H.: Occupational Leukoderma, Pub. Health Rep. **55**:1111-1130 (June 21) 1940.

CONCURRENT INFESTATION WITH A RARE MITE AND INFECTION WITH A COMMON DERMATOPHYTE

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ANDREW G. FRANKS, M.D.
AND
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MORRIS LEIDER, M.D.
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FORMAL reports of the finding of mites of the genus Dermatophagus on the human skin are very few and rather ancient. Through the kindness of Dr. Edward W. Baker,[1] of the Division of Insect Identification of the Department of Agriculture, who identified the mite in our case, we are able to give the following brief account of the literature, some of which we shall discuss *in extenso* below.

In the foreign literature there is the original communication of Bogdanoff,[2] dated 1864. Bogdanoff named the particular mite we are concerned with Dermatophagoides scheremetewskyi. Some time later it was found again on the skin, in Italy and redescribed. In the American literature there are an early report [3] and related correspondence about it [4] published in 1896. This last-mentioned case is curious in many respects and has surrounding it a somewhat vitiating dispute which we shall explain later.

For the rest, we also know of a current infestation, the report of which is as yet unpublished, in the form of a small domestic epidemic which we will refer to again in the proper place. Recently Dr. Baker informed us that he identified another specimen of this mite, which was found in a bed in Chester, N. H., and which was said to have caused an itch. In Japan [5] Dermatophagi have been discovered,

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1. Personal communications to the authors.

2. Bogdanoff, A.: Deux acariens trouvés par M. Schérémétewsky sur l'homme, Bull. Soc. Imp. d. Nat. de Moscou **37**:341, 1864.

3. Menger, R.: A Singular and Apparently New Skin Disease, Texas M. News **5**:337 (June) 1896.

4. (*a*) Reynolds, H. M.: Letter to the Editors, Texas M. News **5**:494 (Sept.) 1896; (*b*) Menger, R.: Letter to the Editors, Texas M. News **5**:542 (Oct.) 1896.

5. Sasa, M.: Contribution to the Knowledge of Human Acariasis, Nisshin Igaku **34**:167, 1947.

and described under other titles, in the sputum and urine in a case of Loeffler's syndrome.

In the literature of entomology there are accounts of this mite in its zoologic aspects. Again we are indebted to Dr. Baker [1] for most of the following taxonomic, morphological and general entomologic data.

Dermatophagoides scheremetewskyi (Bogdanoff) belongs to the family of Epidermoptidae and is a member of the sarcoptiform group of mites which includes the grain mites (Acaridae or Tyroglyphidae), the itch mites (Sarcoptes) and the feather mites (Analgesidae). The Epidermoptidae as a whole are usually considered to be skin parasites of birds. The accompanying table indicates important structural characteristics, some of which distinguish Dermatophagoides scheremetewskyi from Sarcoptes scabiei.

Some Structural Characteristics of Dermatophagoides Scheremetewskyi and Sarcoptes Scabiei

Body Part	Dermatophagoides Scheremetewskyi *	Sarcoptes Scabiei †
‡ 1. Legs	All legs have ambulacral apparatus (suckers, tarsal stalks or adhesive lobes)	In the female the anterior pairs only are so adorned; the male has them additionally on the fourth (posterior) pair
‡ 2. Setae (bristles)	There are no vertical setae but two pairs of long posterior setae and, on the dorsal surface of the body, paired setae over the mouth parts	The male has only one pair of long prominent posterior setae; the female has two pairs of moderately long posterior setae; there are no dorsal setae over the mouth parts
3. Tegument	The tegument is soft and striated	Same
‡ 4. Shield	There is an anterior dorsal sclerotized shield	In the comparable region, there is the plastron or rugose area (Munro) which is more heavily chitinized and somewhat browner in color than the rest of the tegument
5. Chelicerae (mandibles)	There are chewing chelicerae	Same
‡ 6. Position of anus	The anus is not terminal but is situated higher on the ventral aspect	The anus is terminal
‡ 7. Female form	The female is distinctly rounded	The female is distinctly oval

* These data were supplied by Dr. Baker.
† These data were taken from Friedman, B.: The Story of Scabies, New York, Froben Press, 1947, vol. 1.
‡ The double dagger denotes a distinguishing structural characteristic.

REPORT OF A CASE

F. K., a boy of 15 years, presented an eruption of two years' duration on both soles (fig. 1) and the right palm. The nails of the right thumb and middle finger showed abnormality of equal duration. Clinical examination of the soles and palm revealed a fine, branny, superficial scaling. There were many pinhead-sized papules and vesicles among the scales. In some places scales were arranged in collarettes. The affected nails were lusterless, opaque and deformed; the plates looked grayish yellow. The right middle finger nail had been avulsed twice, but the onychodystrophy recurred each time. Mycologic examination consistently showed hyphae on repeated studies of direct preparations from the nails, palm and soles. Repeated cultures resulted in but one growth of a pathogenic fungus, which was Trichophyton purpureum. Even this positive culture was quickly overgrown by a Penicillium contaminant. Finally, the unexpected and unusual observation was the rare mite (fig. 2) which appeared in a scraping from the soles when cleared in the customary fashion with potassium hydroxide.[6]

6. This preparation was made by our observant technician, Mrs. Frances Karpluk, who called our attention to the surprising mite.

COMMENTS

Bogdanoff [2] brought to the attention of the Western world, through the medium of the French literature, the work of Scheremetewsky of Moscow, who, in an intensive and extensive study of acari, is said to have clearly differentiated Dermatophagoides from the common mite of scabies. Also, Fürstenberg [7] is credited with a detailed general description of the organisms of the genus Dermatophagus.

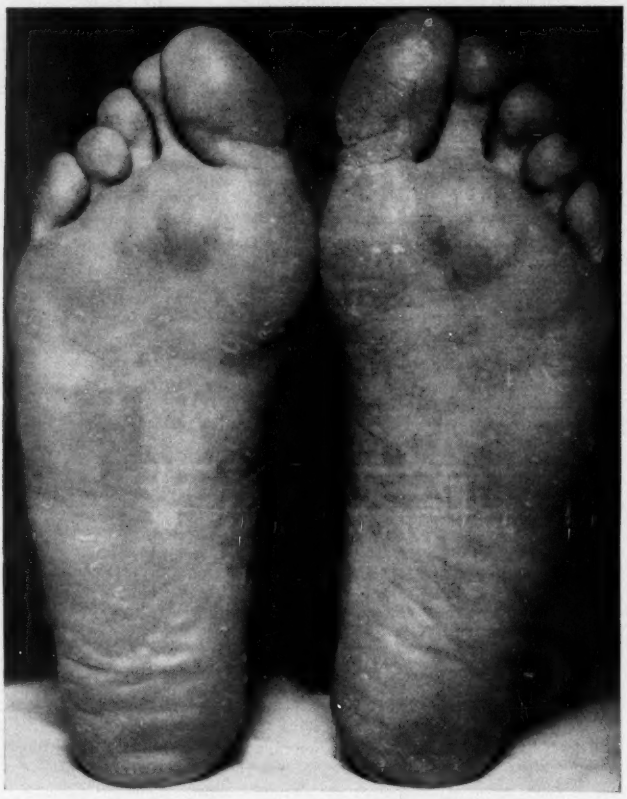

Fig. 1.—Clinical appearance of the eruption on the soles.

The latter author shows that these mites do not burrow (as do the scabietic mites) but feed only on the most superficial epidermal cells, particularly on the partially and fully keratinized cells of the stratum corneum (probably hence the derivations: Dermatophagus, skin eater; Dermatophagoides, like the skin eaters). The dermatophagi thus remove only the uppermost layer of the epidermis to obtain their nourishment and build their dwelling places under the debris of the superficial

7. Fürstenberg, M. H. F.: Die Krätzmilben der Menschen und Thiere, Leipzig, 1861, cited by Bogdanoff.[2]

Fig. 2.—Dermatophagoides scheremetewskyi found in the case herein reported.

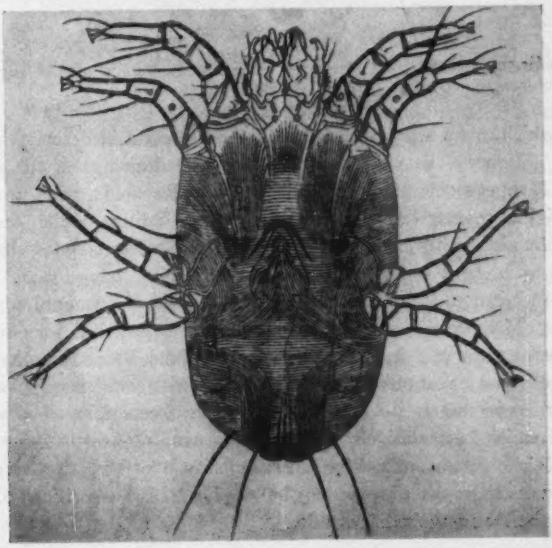

Fig. 3.—Dermatophagoides scheremetewskyi, from Bogdanoff.[3]

epidermis which appears as "scurf." This "scurf" is very easily removed by mere brushing, which easily dislodges the mites. It is very easy to see from the feeding habits, which amount to a nibbling, and from the nesting habits, which are precarious, that these mites must provoke very little inflammation and exudation. Figure 3 is a reproduction of a picture of Dermatophagoides scheremetewskyi from Bogdanoff's article.[2]

The premier American account is by one Menger who, writing in the *Texas Medical News* of 1896,[3] reported a dermatosis which was stated to have occurred in a certain Dr. Reynolds, a retired professor of science. As we have indicated, the circumstances surrounding this report are peculiar. The principals in the case were Texans, and, with the well known bellicosity of those nationals, a lengthy and vigorous logomachy was carried on about the details of the matter. Menger said that the condition in Reynolds consisted of a papular eruption with intense itching and burning of eight months' duration. Scrapings purporting to be from Reynolds' skin were described as consisting of yellowish brown, glittering, sandlike

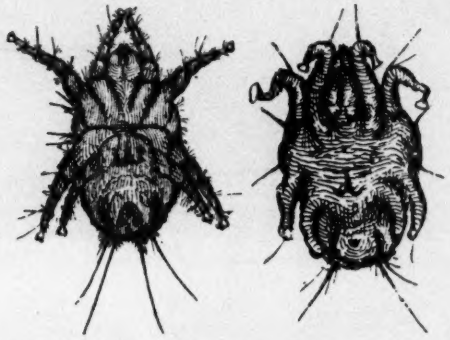

Fig. 4.—Dermatophagoides, from Menger.[4b] These views were said to be engravings made from photomicrographs.

material in which many acari were found that correspond in description to dermatophagoides. Figure 4 shows reproductions of the drawings of the mites which appeared in Menger's rebuttal correspondence [4b] to Reynolds, who, promptly after Menger's original report,[3] denied in a letter [4a] to the Editors of the *Texas Medical News* that Menger's mites came from his body. Reynolds claimed that the mites he submitted to Menger were cheese mites which he had lying around in a jar of lotion of sweet cream (*sic*). From an examination of all communications, it does not seem that Menger was the victim of a tasteless practical joke nor yet that he was the perpetrator of a fraud. Whatever may have been the unknown quantities in the personal equations of the disputants, Menger's description makes it likely in retrospect that he was not dealing with cheese mites but with a new organism for which he tentatively suggested the names "Acarus Incapsulator" or "Sarcoptes Tricho-genetos (Boeking)." Comparison of the engravings (fig. 4) from his photomicrographs with modern knowledge leads authorities [1] to think that he described the Dermatophagoides mite.

Whatever else is known or mysterious about this rare mite, in this country it seems to have a propensity to infest professors and to incite acrimony. It augurs both well and ill for our young patient. For, in addition to the Menger-Reynolds controversy, there is the case of a contemporary professor of zoology in an Eastern university who has a scalp infestation with Dermatophagoides scheremetewskyi. This patient, who prefers anonymity, writes bitterly as follows [8]:

I happen to have been the unfortunate victim of (*a*) a rather severe infestation with the above-mentioned mite and (*b*) the extraordinary ignorance and/or indifference of certain of your colleagues. I refused to accept their diagnosis of "Just your imagination." I captured some of the mites from my scalp and from the scalps of two other members of my family. Failing in an attempt to classify them, I sent them to Dr. Baker. To him thanks are due for identification of the causative agent. The infestation in my scalp and in the scalps of the other two members of my family is now under control. It is no thanks to the medical profession that anything resembling control has been accomplished. The source of the infestation is not known to us.

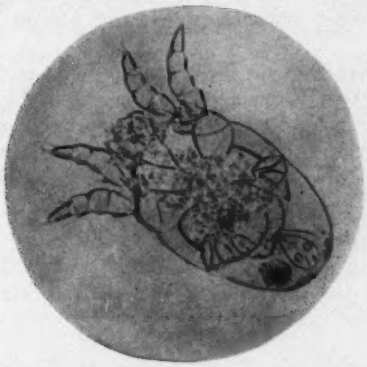

Fig. 5.—Dermatophagoides scheremetewskyi, photograph courtesy of Dr. Manabu Sasa.[5]

We must accept with slightly bowed and repentent heads the strictures of this mismanaged patient. We may take comfort in the thought that a complaint of infestation of the scalp with anything but grossly visible lice would ordinarily suggest a delusion of parasitosis. However, accusation and justification left aside, the questions of pathogenicity, source of infestation and therapy of this acariasis are worthy of some consideration.

The early observers (Scheremetewsky, Bogdanoff) found the mites in conjunction with the much commoner infestation of classic scabies. One specimen was found in a case of impetigo. Our own observation was in a case of dermatophytosis. From all these observations and from an evaluation of the mite's habits, we imagine that its pathogenicity must be small—and facultative at that. The entomologic fact is that mites of this order are obligate parasites on birds (Epidermoptidae bilobatum rivolta is found on chickens and causes a scaly disease), and one may wonder whether fowls (including pets) are not the rare, occasional source of infestation of man and whether an underlying dermatosis (scabies,

8. Personal communication to the authors.

impetigo, dermatophytosis, seborrheic dermatitis?) is not essential for this acariasis to establish itself on the human being.

In the matter of therapy, little is known, probably because experience is so limited. Our severely critical correspondent who suffered from the infestation of the scalp did not reveal her method of control. We would guess that, if scaliness of the scalp were a basic condition in her, control of the dandruff would make it difficult for this acariasis to maintain itself. We ourselves found that 2 per cent salicylic acid in 5 per cent sulfur ointment conferred some benefit on our patient. It would seem from the extremely superficial lodgment and feeble pathogenicity of these mites that ordinary soap and water lavage ought to be sufficient in uncomplicated cases, if such do indeed occur. However, there are examples of exceedingly persistent affliction with torpid organisms in certain mycoses and pyogenic infections. This infestation may be of that type. It would be interesting to know whether veterinary medicine has an effective remedy and whether modern scabieticides like hexachlorocyclohexane (kwell®), 10 per cent crotonyl-N-ethyl-o-toluidide (eurax®) and DDT-ethyl aminobenzoate-benzyl benzoate mixture would be curative.

A final interesting point is the observation of mites of this class within body cavities. Boyd [9] described Turbinoptes strandtmanni in the nasal passages of the gull. This observation may be related to the Japanese discovery of this metazoon in human urine and sputum (see fig. 5). If this organism is capable of enteral or systemic propagation, it may sometime present a serious problem indeed.

9. Boyd, E.: A New Genus and Species of Mite in the Nasal Cavity of the Ring-Billed Gull (Acarina, Epidermoptidae), J. Parasitol. **35**:295 (June) 1949.

RAPID PERMANENT STAINING AND MOUNTING OF SKIN SCRAPINGS AND HAIR

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THERE has been in use in this laboratory for several months a procedure for staining and mounting skin scrapings and hairs which is exceedingly simple and rapid, yields permanent preparations and produces slides of a quality equal to or better than those obtained by more complicated methods.[1] The use of polyvinyl alcohol-lactophenol-cotton blue [2] permits more rapid preparation of "permanent" mounts than does the new method, but fungus structures stained with the PVA medium lose their color quickly and cotton blue so applied penetrates clinical materials poorly. Tinea versicolor scales, prepared by the method about to be detailed, have remained in excellent condition for seven months (fig. 1), as have skin scrapings containing Trichophyton hyphae (fig. 2).

The general procedure will be described first, followed by suggested modifications for different categories of clinical specimens.

A. MATERIALS REQUIRED

The following materials are required for the procedure:

1. Solution of methylene blue hydrochloride, prepared by dilution of 1 part of a saturated 95 per cent alcoholic solution (1.48 Gm. per 100 cc.) of the dye with 9 parts of distilled water
2. Distilled water
3. One per cent solution of acetic acid
4. 1,4-dioxane (Caution: Avoid excessive inhalation of dioxane vapors.)
5. A synthetic resin such as HSR (Harleco synthetic resin, Hartman-Leddon Co., Philadelphia

B. GENERAL PROCEDURE

1. Scrapings (the thinner the better) or hairs are placed directly on a clean microscope slide and covered with 1 to 2 drops of methylene blue solution.
2. The dye is allowed to act for 30 seconds to one minute (longer for very thick specimens) and then is drawn off by means of small torn pieces of bibulous paper.
3. Distilled water is applied with a dropper, permitted to remain until dye ceases to flow from the specimen, and drawn off, as above, to dryness. A second application of water may be necessary for removal of excess dye.
4. In some instances more vigorous decoloration is required for best results. For this, 1 per cent acetic acid is used and drawn off after an appropriate interval and this procedure followed by an application of water.

From the Communicable Disease Center, Laboratory Services, Public Health Service, Federal Security Agency.

1. Muskatblit, E.: Staining of Fungi in Scales and Hairs: Method of Staining with Polychrome Methylene Blue, Arch. Dermat. & Syph. **59**:236-242 (Feb.) 1949.

2. Huber, W. H., and Caplin, S. M.: Simple Plastic Mount for Permanent Preservation of Fungi and Small Arthropods, Arch. Dermat. & Syph. **56**:763-765 (Dec.) 1947.

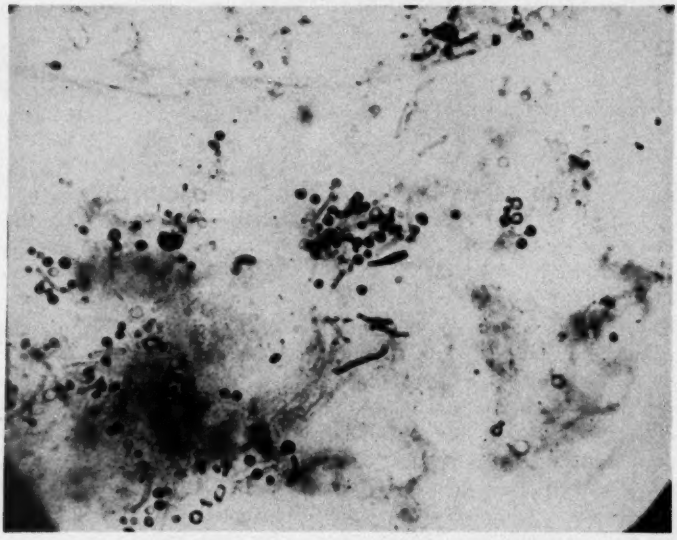

Fig. 1.—Scales from case of tinea versicolor, stained and mounted by methylene blue permanent (MBP) method; original magnification, × 430.

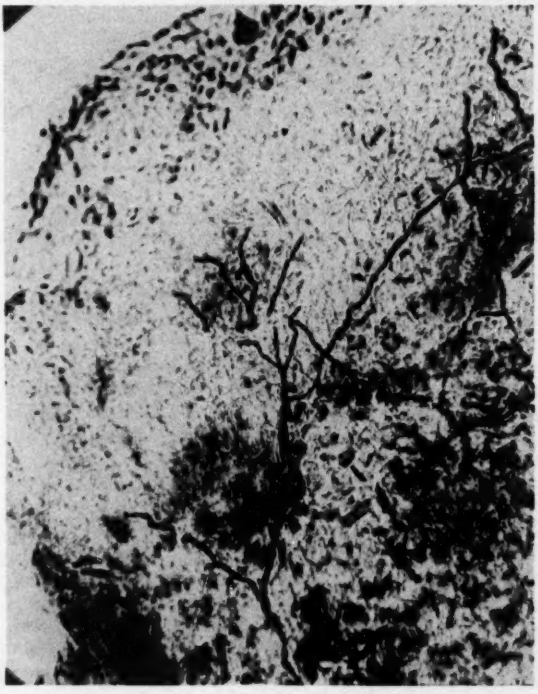

Fig. 2.—Skin scraping from case of trichophytosis, MBP slide; original magnification, × 200.

5. One or 2 drops of 1,4-dioxane are added to dehydrate the specimen. After 5 to 10 seconds, most of this liquid is drawn off.

6. When the remaining dioxane has evaporated almost entirely (evaporation to dryness does not harm the specimen if the next step is not delayed more than a few minutes), a drop of the resin is added and a cover slip applied. Air bubbles are less likely to form if a small drop of the mounting fluid is applied to the apposing surfaces of both the slide and the cover slip and the drops permitted to coalesce before the slip is lowered completely. Pressure on the cover slip will serve to flatten the preparation so that fungus structures are seen more readily.

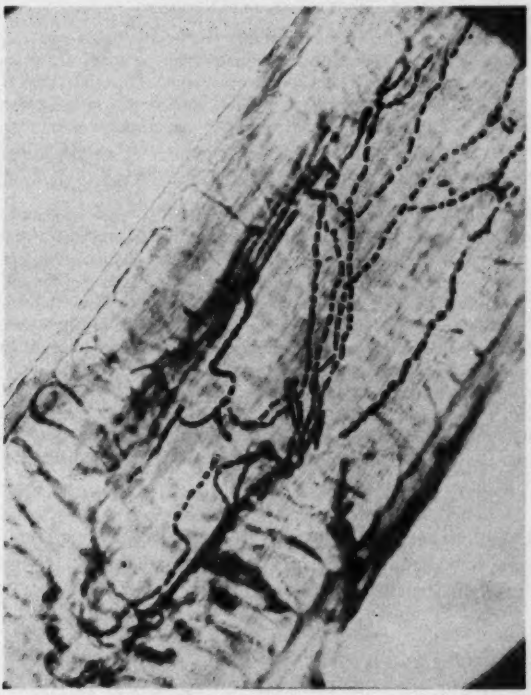

Fig. 3.—Hair from experimental trichophytosis in guinea pig (courtesy of Dr. Lucille K. Georg), MBP slide; original magnification, × 430.

C. SPECIFIC PROCEDURES

Tinea Versicolor Scales (fig. 1).—In the preparation of tinea versicolor scales, apply the stain for 30 seconds; the wash, for 30 seconds, and the dioxane, for 10 seconds. Fungus structures appear deep blue against a light greenish blue background.

Erythrasma Scales.—For the preparation of erythrasma scales, employ the same technic. This method is especially helpful in the routine examination of skin scrapings for Nocardia minutissima (Actinomyces minutissimus) which requires the oil immersion objective, since the use of oil with a wet mount (solution of methylene blue, sodium hydroxide, etc.) presents manipulative difficulties.

Dermatophytes in Scales (fig. 2).—In making slides for the detection of dermatophytes in scales, use the same technic.

Dermatophytes in Hair (fig. 3).—For preparations to show dermatophytes in hair, use the stain 2 minutes, wash 1 minute, acetic acid solution 5 to 10 seconds, wash 1 minute (the

preceding two steps are not always necessary) and dioxane 1 minute. Hyphae and spores stain dark blue; the hair is unstained.

For hairs from trichomycosis axillaris use the following method: stain, 1 minute; wash, 1 minute; acetic acid solution, 5 minutes; wash, 1 minute, and dioxane, 1 minute. Fungus filaments stain dark blue; the gelatinous matrix appears light blue, and the hair is unstained.

Nail Scrapings.—The use of this method for preparations of nails is effective only with extremely thin scrapings, since the dye is slow to penetrate the nail. However, a good permanent mount may be made even though the fungus mycelium be unstained.

D. ADDITIONAL APPLICATIONS

A further modification of the technic permits immediate diagnostic examination of a specimen to be followed by rapid permanent mounting. Skin scrapings are examined in a drop of the methylene blue solution surmounted by a cover slip. This slide then is set aside and allowed to dry (several hours or overnight). Water, applied with a dropper to the edges of the cover slip, moves by capillarity through the entire preparation and loosens the cover slip so that it may be removed. Since a portion of the scales usually adheres to both slide and cover glass, each may be used to prepare a permanent mount, with cover glass and slide, respectively, as in steps 3, 5 and 6 above.

When material is abundant, the method may be adapted to mass production of permanent mounts, for use in teaching and other purposes. A quantity of scrapings or hairs is placed in the bottom of a tapered centrifuge tube. Methylene blue solution sufficient to cover the material is mixed well with it by means of a thin glass rod or pipet and the mixture permitted to stand for 15 minutes. The tube is centrifuged at 2,000 rpm for 5 minutes and the supernate drawn off with a capillary pipet. (If a centrifuge is not available a longer period of standing may be employed to permit adequate sedimentation.) The tube then is filled with distilled water, which is mixed thoroughly with the specimen, allowed to remain for 5 minutes and removed as above. Enough dioxane is added to more than cover the residue and is mixed with it thoroughly with a dry pipet. Almost all the dioxane subsequently is removed, leaving just enough to facilitate distribution of the scales or hairs to a number of slides. After evaporation to near-dryness of the dioxane on each slide, a drop of the resin is added and a cover slip applied.

SUMMARY

A method, with several modifications to suit diverse purposes, is described for rapid staining and mounting of hairs and skin scrapings. It yields permanent slides in which fungus structures stand out clearly against the substrate.

HISTOPATHOLOGY OF THE NODOSE LESIONS OF THE LOWER EXTREMITIES

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NODOSE lesions of the lower extremities are most frequently due to inflammatory reactions which are primarily localized in the subcutaneous fat, its connective tissue septums and blood vessels. The changes in the overlying cutis and epidermis are secondary to those in the subcutaneous fat and its septums and vessels. These nodes and lesions have an intense central reaction which gradually recedes at the periphery, with the formation of the indistinct borders observed clinically.

Atrophic changes in the fat lobules were classified into four types by Flemming in 1871, according to Schidachi.[1] The first type is simple atrophy, in which the individual cells become smaller. The contained fat globules are smaller, and thus the volume of fat cells in the fat lobule is diminished. The second type is the result of liquefaction or serous degeneration. In this sort of change the fat globule becomes smaller. A serous substance is found between it and its membranous border. The third type is replacement by proliferative atrophy, previously called "Wucheratrophie." In this variety the fat globules are reduced in size but the cellular cytoplasm contains increased numbers of nuclei. Thus, at the expense of shrinking fat cells, the previously occupied area is replaced by increased nuclear elements in the cellular and intercellular areas of the fat lobules. The fourth type is that in which there is fibrosis.

These atrophic changes in the fat may be found most frequently in combinations, e. g., simple and serous, serous and proliferative, or proliferative and fibrotic. The predominating type determines the classification of the atrophy.

Vascular involvement, difficult to demonstrate at times, can be found in many of these nodose lesions. Involved arteries and veins can be seen in the center of the node. Sometimes the specimen removed for biopsy has not included material from the involved blood vessel, and at other times the tissue has not been sectioned in the proper site, so that more sections must be made and examined to find the involved vessels. Changes in the vessel wall are variable. They involve the various layers of the vessel wall by proliferation, infiltration of cellular elements and dissociation due to edema and hyalinization. Proliferation of the

From the Division of Dermatology, University of Southern California, and the Los Angeles County General Hospital.

1. Schidachi, T.: Über die Atrophie des subkutanen Fettgewebes, Arch. f. Dermat. u. Syph. 90:97-130, 1908.

intima may result in complete obstruction of the vessel with resulting gradual, slowly progressive sclerosis and atrophy of the dependent tissues. Inflammatory reaction in the vessel walls may result in thrombosis and sudden occlusion of the vessel with rapidly progressive necrosis of the adjacent tissue. Thus, our premise is that nodular lesions arise when vasculitis and panniculitis result in fibrosis. Ulceration of the epidermis and cutis is secondary to the changes as enumerated.

Fig. 1.—Erythema nodosum (× 100). Involvement of the interlobular septum in the subcutaneous fat may be seen. In the center is a dissociated artery with the characteristic arteritis. To the left are nests of polymorphonuclear cells. Throughout the septum is a serous exudate as well as a cellular infiltrate.

The histopathological features observed in study of erythema nodosum associated with proved cases of coccidioidomycosis, tuberculosis, rheumatic infection, tularemia, pregnancy and the administration of sulfathiazole were the same, regardless of the associated disease. Erythema induratum, relapsing febrile nodular nonsuppurative panniculitis and periarteritis nodosa were three other types of lesions studied histopathologically. All four of these conditions will be compared with each other.

ERYTHEMA NODOSUM

Erythema nodosum showed arterial changes consistent with periarteritis nodosa. The characteristic vascular changes have been considered as allergic or hypersensitive angiitis by Bergstrand,[2] Zeek, Smith and Weeter[3] and Middelmis.[4] Because the vessel walls showed changes similar to those of periarteritis nodosa of the nonfatal type, one must consider these changes to be of a vascular nature, closely related to but not identical with the panarteritis type of polyarteritis nodosa.

In addition to the vascular changes, the interlobular septums of the subcutaneous fat are infiltrated by nests of polymorphonuclear cells in some areas; in other areas, especially those adjacent to the fat cells, there are lipophagic histiocytes and an occasional foreign body giant cell. In still other areas edema and moderate eosinophilic cell infiltrate are seen. Hyalinization of the connective tissue of the septums is also evident. The fat cells show normal thin intercellular networks. Occasional cells are ruptured and undergoing liquefaction degeneration. Bergstrand[5] and Löfgren and Wahlgren[6] have reported similar changes. In two cases in the present study radiating nodes were seen as described by Miescher.[7] Ophüls[8] reported the observation of similar nodes in periarteritis nodosa. Miescher was unable to associate these nodes with blood vascular structures but thought them to be of reticulum origin. These nodes radiated from a central unlined space. However, I could not prove that these cells were not nests of adventitia cells cut from an angulated tortuous blood vessel. In spite of all these changes, fibroblastic proliferation is practically negligible. Fat atrophy is very slight, so that healing occurs without any surface change or depression.

Lipophagic granulomas secondary to fat necrosis caused by subcutaneous infections and perivenous extravasations of vein-sclerosing solutions must be differentiated. They are characterized by an associated infiltrate of lipophagic histiocytes and Touton giant cells surrounded by a pleomorphous infiltration of polymorphonuclear cells, lymphocytes and fibroblasts. The necrosis involves the entire fat lobule, and fibrosis is a dominant feature of the histological picture.

ERYTHEMA INDURATUM

Erythema induratum is a tuberculous vasculitis of the subcutaneous vessels. Earliest sections have shown epithelioid cell tubercles progressing from the vessel wall. In the blood vessels gradual proliferation of the intima completely occludes the vessel and it becomes barely visible as a definite structure, appearing as a

2. Bergstrand, H.: Is Erythema Nodosum a Hypersensibility Reaction of Anaphylactic Type? Acta dermat.-venereol. **29**:539-543, 1949.

3. Zeek, P. M.; Smith, C. C., and Weeter, J. C.: Studies on Periarteritis Nodosa: III. The Differentiation between the Vascular Lesions of Periarteritis Nodosa and of Hypersensitivity, Am. J. Path. **24**:889-919, 1948.

4. Middelmis, J. H.: Erythema Nodosum, Brit. J. Radiol. **22**:375-383, 1949.

5. Bergstrand, H.: Morphological Equivalents in Polyarthritis Rheumatica, Periarteritis Nodosa, Transient Eosinophilic Infiltration of the Lung and Other Allergic Syndromes, J. Path. & Bact. **58**:399-409, 1946.

6. Löfgren, S., and Wahlgren, F.: On the Histo-Pathology of Erythema Nodosum, Acta dermat.-venereol. **29**:1-13, 1949.

7. Miescher, G.: Zur Histologie des Erythema nodosum, Acta dermat.-venereol. **27**:447-468, 1947.

8. Ophüls, W.: Periarteritis Acuta Nodosa, Arch. Int. Med. **32**:870-898 (Dec.) 1923.

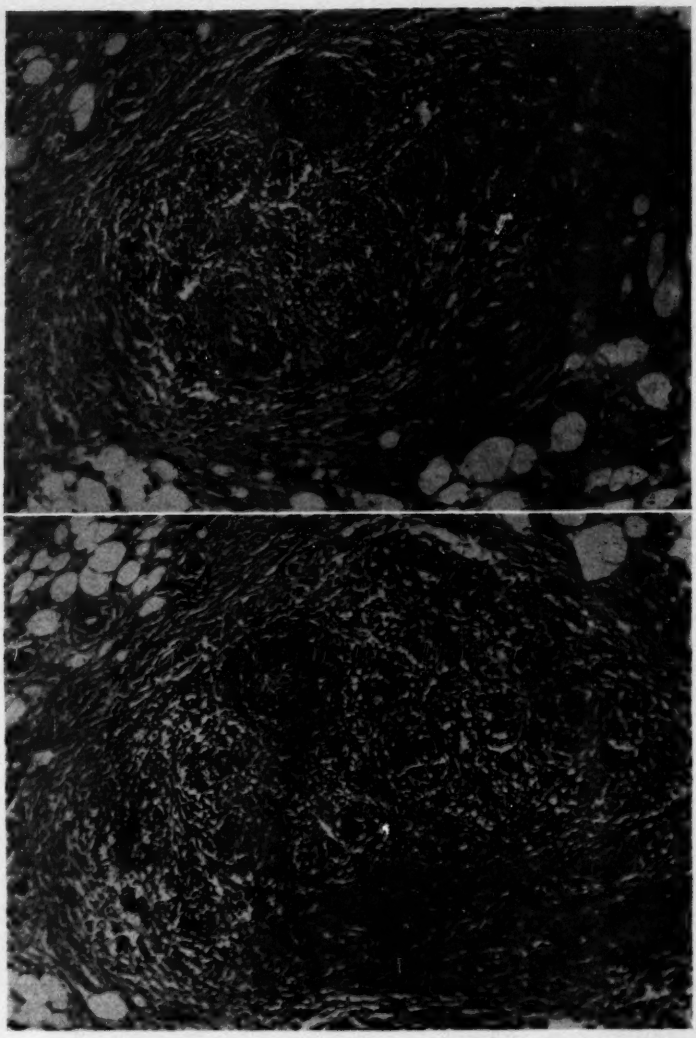

Fig. 2.—Erythema induratum (× 100). Upper photograph, of a section stained with hematoxylin and eosin. The fat lobule in the center has been replaced by a tuberculoid granuloma. Giant cells are at the bottom to the right. An obliterated artery is seen above the center. The lower photograph shows the same section as the upper one, but stained with elastic stain. The double elastic lamina in the occluded artery may be observed.

rounded, lamellated eosinophilic mass in a mantle of lymphocytes. This mantle of lymphocytes intermingles with the fat cells, increased nuclear elements between them resulting. Consequently the fat globules diminish in size, and, ultimately, fibrosis almost completely replaces the fat. The central vessel is most easily discovered by the use of an elastic tissue stain, which shows the residual definite elastic lamina and indicates the existence of a previously functioning vessel. In erythema induratum the normal architecture of subcutaneous fat is obliterated by the replacement ("Wucher") atrophy, which in turn is followed by fibrosis. Necrosis of the cutis and ulceration of the epidermis are frequently found in this condition because of the complete vascular occlusion and the resultant loss of nutrition. Ulceration, replacement ("Wucher") atrophy and fibrosis result in clinical depressed scar formation.

Nodular vasculitis of Montgomery, O'Leary and Barker [9] is identical, histologically, with erythema induratum, but in it no clinical evidence of tuberculosis can be found. It is presumed to be due to involvement of vessels by some noxae in patients with sluggish circulation, clinically evidenced by cold, clammy extremities.

One can differentiate Darier-Roussy sarcoid from erythema induratum, even though many believe that the conditions are identical. Histologically, in Darier-Roussy sarcoid only lymphocytic infiltration is seen in the lower part of the cutis. The condition is mainly localized in the fat lobules. The septums show very slight changes. The infiltrate is predominantly lymphocytic with a few polymorphonuclear leukocytes, histiocytes, fibroblasts and an occasional giant cell. It is grouped in masses with areas of normal fat interspersed with the lobule. These patchy arranged nests of replacement ("Wucher") atrophy involve the fat lobule, the picture being unlike the diffuse distribution seen in erythema induratum. Foci of fat necrosis are much less evident than in erythema induratum and are not usually found.

RELAPSING FEBRILE NODULAR NONSUPPURATIVE PANNICULITIS

Relapsing febrile nodular nonsuppurative panniculitis is also one of the nodose lesions seen on the lower extremities. Pfeifer,[10] Gilchrist and Ketron,[11] Weber [12] and Christian [13] have described the clinical and histological characteristics of this condition. The predominant clinical feature is the healing of the nodules with resulting surface depression due to the local loss of subcutaneous fat.

On histological examination the cutis shows very slight changes, there being only a mild lymphocytic perivascular infiltration. However, entire fat lobules are involved in the subcutaneous fat. The septums between the fat lobules show very

9. Montgomery, H.; O'Leary, P. A., and Barker, N. W.: Nodular Vascular Diseases of the Legs: Erythema Induratum and Allied Conditions, J. A. M. A. **128**:335-341 (June 2) 1945.

10. Pfeifer, V.: Über ein Fall von herdweiser Atrophie des subcutanen Fettgewebes, Arch. f. klin. Med. **50**:438-449, 1892.

11. Gilchrist, T. C., and Ketron, L.: A Unique Case of Atrophy of the Fatty Layer of the Skin, Preceded by Ingestion of Fat by Large Phagocytic Cells—Macrophages, Bull. Johns Hopkins Hosp. **27**:291-294, 1916.

12. Weber, F. P.: A Case of Relapsing Non-Suppurative Nodular Panniculitis Showing Phagocytosis of the Subcutaneous Fat Cells by Macrophages, Brit. J. Dermat. **37**:301-311, 1925.

13. Christian, H. A.: Relapsing Febrile Nodular Non-Suppurative Panniculitis, Arch. Int. Med. **42**:338-351 (Sept.) 1928.

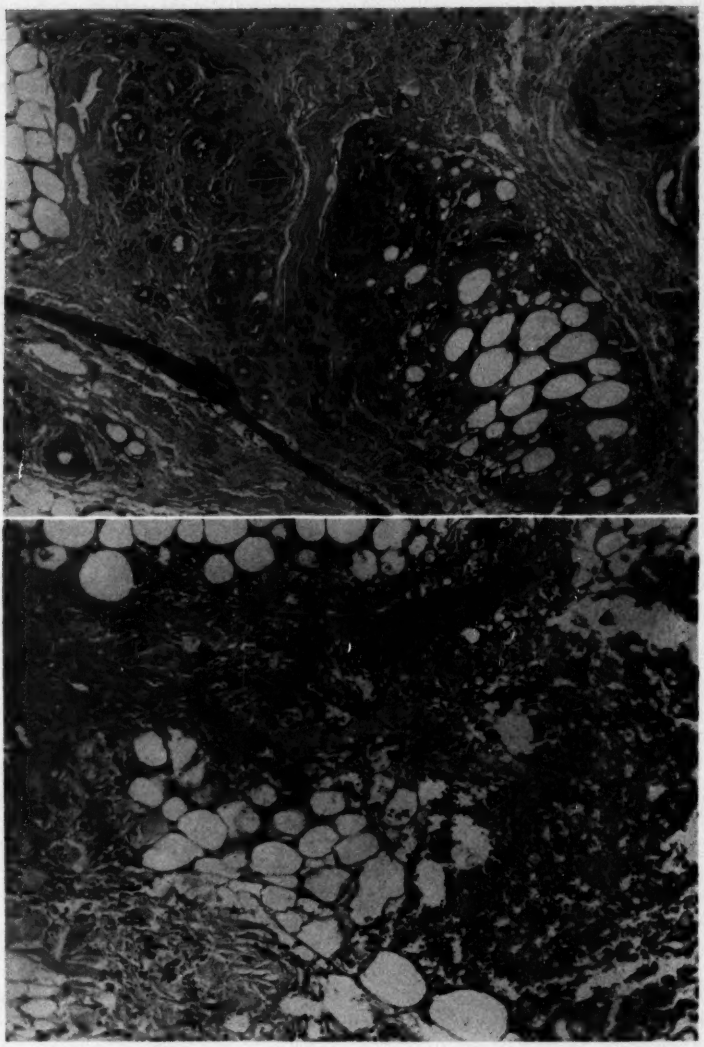

Fig. 3.—Recurrent nonsuppurative nodular panniculitis (× 100). In the upper photograph the fat lobule has been replaced by serous edema. To the left of this lobule edematous occlusion of a blood vessel is seen. Above and to the right of the fat lobule a nerve has been sectioned. To the right is necrosis of the fat lobule. At the top infiltration of the septum and lipophagic histiocytes are seen at the fat lobule border.

slight changes and scanty cellular infiltration. The reticulated structure of the fat lobules has disappeared. No nests of cellular infiltration are seen. The fat cells are surrounded at the periphery by lipophages whose protoplasm has a reticulated structure, and thus the involved lobule resembles a glandular acinus. Occasionally lipophagic giant cells having a reticulated structure are seen. Vessel changes are rare, but where found they consist characteristically in an edematous obliterative endarteritis. As a result of this vascular change, areas of fat necrosis occur. This fat necrosis shows no cellular infiltration of a suppurative nature.

Subcutaneous fat necrosis of the newborn is differentiated from nonsuppurative panniculitis by the greater numbers of foreign body giant cells and the elongated needle-like crystals of palmitin arranged in fan shape or rosettes. These crystals are unlike normal fat cells in that they are stained pink by the eosin of the hematoxylin-eosin stain.

Panniculitis is an all-inclusive term subdivided by Keil [14] into primary and secondary groups.

In the primary group were included both febrile and afebrile types of idiopathic fat atrophy, and the secondary group contained a diffuse variety of lesions, such as erythema nodosum, erythema induratum, dermatomyositis, acute lupus erythematosus, scleroderma and the lipophagic foreign body granulomas. If we accepted this classification we would have an unwieldy, unrelated and dissimilar group of conditions, whose only similarity would be involvement of the subcutaneous fat, classified together.

Ulceration and suppuration have been considered as associated with some of the cases of nonsuppurative panniculitis because cultures of these lesions have been sterile. The great majority of these ulcerative lesions fall into the group of allergic or hypersensitive angiitis, which is related to and placed in the nosological position between erythema nodosum on one hand and periarteritis nodosa on the other, as in the classification by Carol, Prakken and van Zwijndregt.[15] Necrosis and ulceration are frequently seen in allergic or hypersensitive angiitis.

PERIARTERITIS NODOSA

Periarteritis nodosa of the skin does not have a single clinical picture. It may be nodular, purpuric, gangrenous or manifest combinations of any of these three forms. This fact accounts for the variability of the histopathological observations. The purpuric and gangrenous forms are similar histologically in that thrombotic processes in the vessels of the skin are evident. The muscularis of the vessel wall shows greatest degenerative changes. The intima is thickened. Beneath it one sees on elastic staining an incomplete lamina elastica interna. The adventitia is broadened and shows two zones of involvement. The inner zone surrounds the necrotic media. This zone contains an infiltration consisting of histiocytes and polymorphonuclear cells. The outer zone of the adventitia appears necrotic in that it has lost its structural recognition. This condition is a focal vasculitis in which there is fibrinoid necrosis of the media and adventitia. The

14. Keil, H.: Panniculitis: Its Place in Nosology, Brit. J. Dermat. **47**:512-521, 1935.

15. Carol, W. L. L.; Prakken, J. R., and Van Zwijndregt, H. A.: Erythema Nodosum und "Relapsing Febrile Nodular Non-Suppurative Panniculitis," Arch. f. Dermat. u. Syph. **182**:329-366, 1941.

loss of the external elastic lamina as observed with elastic stain has been indicative of periarteritis nodosa to some. Occasionally acute disseminated lupus erythematosus and dermatomyositis may show similar vascular changes. Most frequently involved are the arteries of muscular type rather than arteries of elastic type. Aneurysmal bulgings of the vessel walls are difficult to observe in the skin; the fatty tissue undergoes very slight replacement ("Wucher") atrophy but rather is involved by serous atrophy of the cells. Xanthoma-like formations containing vacuoles are arranged in a pseudoglandular fashion around these atrophic fat cells. Numerous giant cells may also be observed. Occasionally aneurysms of the small

Microscopic Picture in Nodose Lesions of the Lower Extremities

	Erythema Nodosum	Erythema Induratum	Nodular Febrile Nonsuppurative Panniculitis	Periarteritis Nodosa
Epidermis and upper part of cutis	Not involved	May have areas of necrosis and ulceration	Mild involvement	Hemorrhage and necrosis
Lower part of cutis	1. Mild polymorphonuclear cell infiltrate 2. Mild edema 3. No necrosis	1. Diffuse lymphocyte infiltrate 2. Caseation necrosis	1. Mild perivascular lymphocyte infiltrate and edema 2. Anuclear caseation necrosis	1. Diffuse lymphocyte infiltrate 2. Perivascular necrosis
Subcutaneous interlobular septums	1. Arteritis, acute a. Dissociation type b. Nonobstructed 2. Nests of polymorphonuclear cells 3. Eosinophilic cells 4. Reticuloendothelial nodules (Miescher) 5. Perilobular giant cells 6. Fibrillary degeneration	1. Obliterative organized thrombotic vasculitis 2. Chronic lobulated granuloma a. Epithelioid b. Giant cells c. Lymphocyte border d. Fibroblastic proliferation 3. Caseation necrosis	1. Arteritis, edematous type 2. Syncytial edema 3. Sparse cell infiltrate	1. Arterial obstruction a. Thrombosis b. Sectoral and segmental involvement c. Intimal proliferation d. Partial loss of lamina elastica interna e. Media dissociated by edema and cell invasion f. Pleomorphous cell infiltrate 2. Collagen necrosis
Fat lobule	1. Normal size 2. Intact—no necrosis	1. Shrunken 2. Replacement atrophy nuclear increase ("Wucheratrophie") 3. Caseation necrosis	1. Entire lobule involved 2. No nuclear increase 3. Serous necrosis of fat cells (lobule looks like sebaceous gland) 4. Phagocytic histiocytes and giant cells	1. Liquefaction of fat 2. Caseation necrosis of collagen
Terminal fibrosis	None No scar	Diffuse cutis and subcutis fibrosis Depressed scar	Diffuse cutis and subcutis fibrosis Depressed scar	Perivascular fibrosis Calcinosis Depressed scar

vessels can be observed. The fibrinoid degeneration of the vessel wall involves only a linear segment of the vessel, and in the segment involved the changes are manifest only in a sector of the wall rather than in its entire circumference. This fibrinoid change may be replaced by calcium deposits. Fibrinoid necrosis has been considered an expression of an allergic reaction. With only skin involvement and no internal organ involvement the prognosis of periarteritis nodosa is good.

Granulomas with and without central necrosis were observed by Bergstrand,[5] Rich [16] and others. These resembled Aschoff's nodules. Ophüls believed the condition started in the adventitia and extended inward, soon involving all the

16. Rich, A. R.: The Role of Hypersensitivity in Periarteritis Nodosa as Indicated by 7 Cases Developing During Serum Sickness and Sulfonamide Therapy, Bull. Johns Hopkins Hosp. **71**:123-135, 1942.

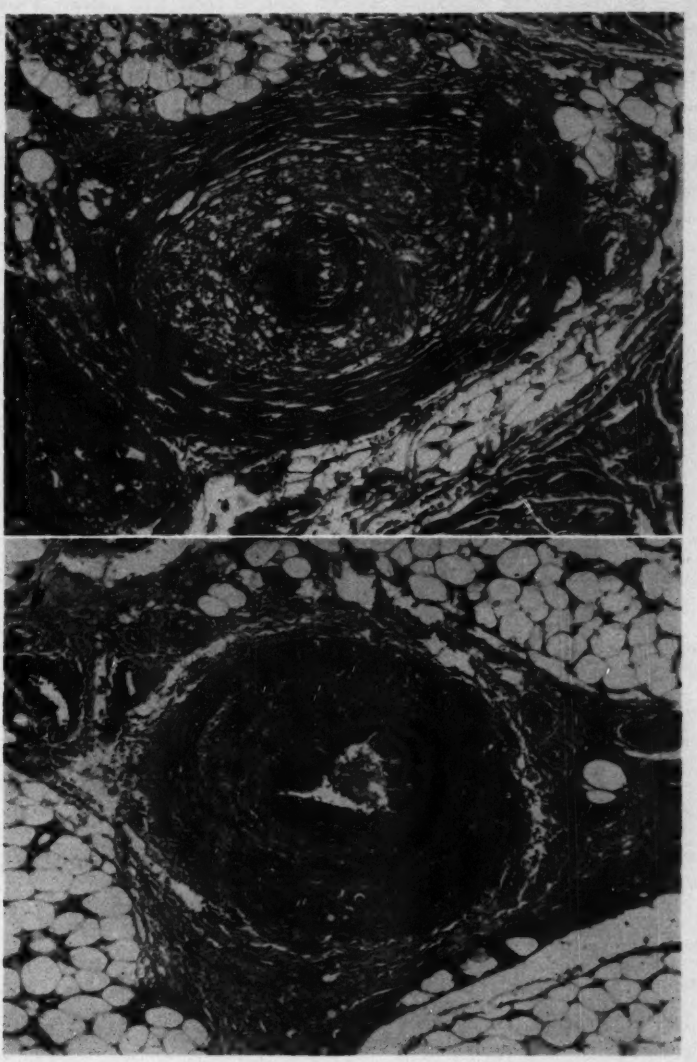

Fig. 4.—Upper photograph, periarteritis nodosa (× 100), from a fatal case. The degenerated, obliterated artery may be observed in the septum of the subcutaneous fat. There is necrosis to the left of the artery. Lower photograph, periarteritis nodosa, benign (× 50). The muscularis and adventitia are dissociated, and the intima has proliferated, partially occluding the vessel lumen. The collagenous tissue of the septum is hyalinized. The vessel wall is invaded by cellular infiltrate.

coats of the vessel. He stated that Aschoff thought there was a great similarity between periarteritis nodosa and the rheumatic nodules. Periarteritis nodosa of the skin heals with scar formation, especially evident adjacent to the vessel.

Necrobiosis lipoidica diabeticorum, granuloma annulare and localized nodular myxedema can at times appear as nodose lesions on the lower extremities. These conditions show degenerative changes of the collagenous fibers of the cutis rather than primary inflammatory involvement of the subcutaneous fat. Necrobiosis lipoidica diabeticorum shows, histologically, replacement of the collagen fiber

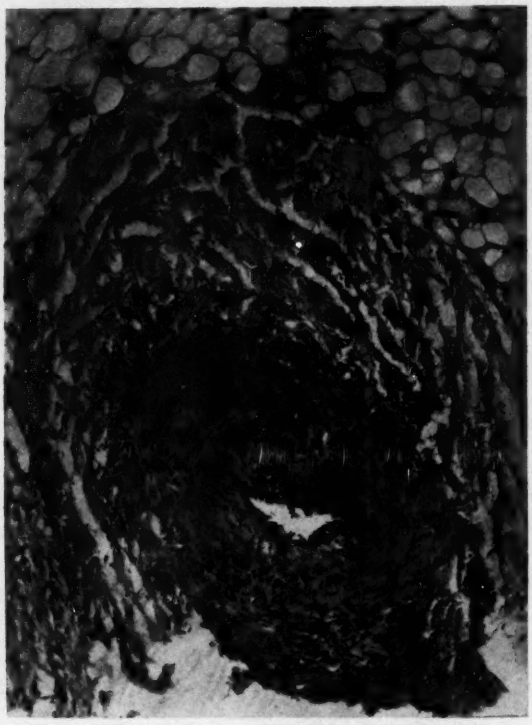

Fig.5.—Old, healed periarteritis nodosa (× 100). Increased deposits of fibrous connective tissue adjacent to the vessel and intense fibrosis of the vessel wall may be seen.

fasciculi by neutral fat in the lower part of the cutis. An infiltrate, consisting of Langhans' giant cells, histiocytic monocytes, lymphocytes and polymorphonuclear cells, is seen adjacent to the degenerated collagen. The blood vessel walls are thickened and hyalinized. The subcutaneous fat is practically uninvolved.

Granuloma annulare is characterized histologically by anuclear, eosinophilic, irregular, stellate masses of degenerated collagen in the cutis. These masses are surrounded by a border of fibroblasts or epithelioid cells. Occasionally giant cells are seen in the bordering cellular infiltrate. The vascular changes seen in necrobiosis lipoidica diabeticorum are not found.

In localized nodular myxedema the solid texture of the collagen fibrils is replaced by a loose, lacelike network of cells with angulated nuclei. These cells have clear cytoplasm and fibrillary cellular borders. Irregular masses of degenerated mucin-like collagen are seen in the midst of these transformed cells.

The nodose lesions of syphilis are difficult to recognize in the differential diagnosis. The subcutaneous fat lobules, the interlobular septums and the lower part of the cutis are, as a rule, all involved simultaneously. Proliferation of the intima of blood vessels is observed throughout the section. A perivascular cellular infiltrate, consisting predominantly of plasma cells, obliterates the adventitial border of these blood vessels. Occasionally areas of necrosis and fibrosis, surrounded by an infiltrate of epithelioid cells, Langhans' giant cells, lymphocytes and plasma cells, are seen. Clinical and serologic confirmation of syphilis is needed to corroborate a histological diagnosis of syphilis.

CONCLUSIONS

The histopathological changes of the inflammatory nodose lesions have been compared as to location, type of reaction and sequelae. Differences which can be the identifying diagnostic criteria are evident in the great majority of cases.

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DISCUSSION

Dr. Eugene M. Farber, San Francisco: Because nodose lesions of the legs differ so little in their clinical appearance, the establishment of an accurate diagnosis depends on careful microscopic study. Dr. Winer has presented a useful synthesis of the histopathology of erythema nodosum, erythema induratum, periarteritis nodosa and the Weber-Christian disease. There is little that can be added to this excellent presentation.

Of particular importance in the study of nodose lesions of the legs is the method of biopsy. Punch biopsy is unsatisfactory because the pathologic changes are deep and diagnosis depends on the presence of blood vessels. The specimen should be obtained by excision of the entire node whenever possible. Even with excision biopsy the slide may be nondiagnostic. As Dr. Winer has mentioned, multiple sections of wide, deep specimens including the subcutaneous tissue may be necessary before a diagnostic section is found. This point is especially true in erythema induratum, where several sections must be studied before typical tubercles are observed.

I would like to add another cause for nodose lesions of the legs, i. e., thrombophlebitis migrans. This occurs in 40 per cent of all patients with Buerger's disease. The lesions are discrete and nodular and are difficult to differentiate clinically from erythema nodosum. Microscopic study reveals profound inflammatory changes in a venule with lesser changes in the accompanying arteriole. There is little necrosis in the adjacent fat.

The microscopic picture of nodose lesions depends to a great degree on the profundity or rapidity of occlusive vascular changes. In erythema nodosum, though the arterioles are stenotic, they are still functional, and hence there is less necrosis of segments of the fat in erythema nodosum than in erythema induratum. I have not been able to demonstrate arteriolar changes except on rare occasions in study of the Weber-Christian disease. If the extensive fat necrosis is not primary, it may be due to sudden or very rapid occlusion of small arteries deep in the subcutaneous tissue or under the fascia.

Dr. Winer has tabulated in his written text a practical and useful comparison of the microscopic features of nodose lesions. I have enjoyed the privilege of studying his material and discussing this fundamental work.

Dr. B. E. Konwaler, Chief of Pathology, Birmingham Veterans Hospital, contributed in the preparation of this paper.

Photomicrography was done by Lloyd Matlovsky.

Tissue preparation and staining were done by Avis Gregersen.

SEBORRHEIC KERATOSIS AND VERRUCA, WITH SPECIAL REFERENCE TO THE MELANOTIC VARIETY

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CHICAGO

THE DISORDER which is currently called seborrheic keratosis in the United States has been described by a multitude of authors under almost as many names (table 1).

TABLE 1.—*Nomenclature of the Disease Currently Called Seborrheic Keratosis in the United States*

Virchow (Die Krankhaften Geschwülste, Berlin, A. Hirschwald, 1864-65, vol. 2)	1864	Simple melanoma
Neumann [6]	1869	Wartlike excrescence
Barthélemy (Ann. de dermat. et syph. **2**: 535, 1881)	1881	Multiple senile papillomas; seborrhea nigra; verrucae planae seniorum
Handford (Illustr. M. News **1**: 293, 1888)	1888	Stearrhea nigricans
Crocker (Diseases of the Skin, ed. 2, Philadelphia, The Blakiston Company, 1888)	1888	Keratosis pigmentosa
Pollitzer [10]	1890	Seborrheic wart
Brocq [9]	1890	Greasy crusts of the glabrous skin
Unna [8]	1896	Seborrheic nevus (seborrheic wart); acanthoid hard nevus (?); keratotic hard nevus (?)
Montgomery (Philadelphia M. J. **1**: 211 [Jan. 29] 1898)	1898	Senile patches (including senile keratosis)
Dubreuilh [29a]	1904	Generalized verrucae planae
Audry (in Besnier, Brocq and Jacquet: La Pratique dermatologique, Paris, Masson & Cie, 1904)	1904	Senile seborrhea (second variety)
Waelsch [26]	1905	Acanthosis verrucosa seborrhoica
Jadassohn [15]	1914	Benign epithelioma; infectious epithelioma
Dawson (Edinburgh M. J. **32**: 501 [Oct.] 1925)	1925	Benign melanoma
Castellani (J. Trop. Med. **28**: 1 [Jan. 1] 1925)	1925	Dermatosis papulosa nigra (in Negroes)
Bloch (Arch. f. Dermat. u. Syph. **153**: 20, 1927)	1927	Non-nevoid melanoepithelioma
Frieboes (in Riecke: Lehrbuch der Haut- und Geschlechtskrankheiten, Jena, G. Fischer, 1931)	1931	Verrucae seniles seborrhoicae
Becker [24]	1932	Epithelioma
Kaiserling (in Jadassohn: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1932, vol. 12, part 2)	1932	Acanthoid pseudonevus; keratoid pseudonevus
Sutton and Sutton [23]	1939	Squamous cell keratosis (for some tumors)
Fox (Arch. Path. **36**: 195 [Aug.] 1943)	1943	Pigmented papilloma
Percival, Drennan and Dodds (Atlas of Histopathology of the Skin, Baltimore, Williams & Wilkins Company, 1947)	1947	Nevus pigmentosus; melanoma
Stewart and Bonser (J. Path. & Bact. **60**: 21, 1948)	1948	Squamous papilloma

The clinical picture is familiar to all dermatologists and has been described by Becker and Obermayer,[1] Ormsby and Montgomery,[2] Sutton and Sutton,[3] Freudenthal and Spitzer,[4] MacKee and Cipollaro [5] and many others.

From the Section of Dermatology, School of Medicine, University of Chicago.

Read at the Seventieth Annual Meeting of the American Dermatological Association, Jasper National Park, Alta., Canada, June 20, 1950.

1. Becker, S. W., and Obermayer, M. E.: Modern Dermatology and Syphilology, ed. 2, Philadelphia, J. B. Lippincott Company, 1947.

AGE OF PATIENTS WITH SEBORRHEIC KERATOSIS

Neumann's association [6] of this condition with senile changes in the skin implied that the disorder was one of senescence. Miescher, Häberlin and Guggenheim [7] showed that some of the pigmentary spots of old people were primitive seborrheic keratoses. However, Unna [8] gave as one reason for the use of the designation "seborrheic verruca" as opposed to "senile verruca" the fact that these lesions are found in people who are not old. Brocq [9] found them in young persons. Pollitzer [10] reported that they had not been seen before the age of 40. Lortat-Jacob [11] stated that they are especially common in women around 50 years of age and are rare before 30. Stelwagon [12] reported the case of a man about 35 or 40 years old with disseminated lesions associated with tendency to epithelial growth and degeneration and dryness and thinning of the skin as seen in xeroderma pigmentosum. Gottheil [13] reported the case of a woman, aged 37, who had had seborrheic keratoses since the age of 30. They were increasing rapidly in number. Darier [14] stated that the tumors can develop before the age of 30. Jadassohn [15] emphasized the importance of predisposition and reported the cases of a mother and two daughters in whom tumors had developed between 20 and 30 years of age. Oliver demonstrated an adult Negro at the Chicago Dermatological Society, on April 19, 1950, with multiple pedunculated seborrheic keratoses which had appeared at the age of 13 and had been growing recently.

Perhaps the earliest reported onset of disseminated seborrheic keratoses was in a patient first presented by Wolff [16] at the sixth Congress of the German Dermatological Society, in May 1898, with the diagnosis of atypical acanthosis nigricans.

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2. Ormsby, O. S., and Montgomery, H.: Diseases of the Skin, ed. 7, Philadelphia, Lea and Febiger, 1948.

3. Sutton, R. L., and Sutton, R. L., Jr.: Handbook of Diseases of the Skin, St. Louis, C. V. Mosby Company, 1949.

4. Freudenthal, W., and Spitzer, R.: Verruca Senilis, in Jadassohn, J.: Handbuch der Haut- und Geschlechskrankheiten, Berlin, Springer-Verlag, 1933, vol. 13, pt. 3.

5. MacKee, G. M., and Cipollaro, A. C.: Cutaneous Cancer and Precancer: A Practical Monograph, New York, American Journal of Cancer, 1937.

6. Neumann, I.: Über die senilen Veränderungen der Haut des Menschens, Sitzungsb. d. Akad. d. Wissench. zu Wein **59**:47, 1869.

7. Miescher, G.; Häberlin, L., and Guggenheim, L.: Über fleckförmige Alterspigmentierungen: Ihre Beziehungen zur melanotischen Präcancerose und zur senilen Warze, Arch. f. Dermat. u. Syph. **174**:105, 1936.

8. Unna, P. G.: The Histopathology of the Diseases of the Skin, translated by Norman Walker, New York, The Macmillan Company, 1896.

9. Brocq, L. A. J.: Traitement des maladies de la peau avec un abrégé de la symptomatologie, du diagnostic et d'étiologie des dermatoses, Paris, 1890.

10. Pollitzer, S.: Die seborrhoeische Warzen (V. Seborrhoica, V. Senilis, V. Plana Seniorum, Keratosis Pigmentosa), Monatsh. f. prakt. Dermat. **11**:145, 1890.

11. Lortat-Jacob, L.: Seborrhoeic Warts, or Verruca Plana Senilis, M. Press **126**:405 (Nov. 14) 1928.

12. Stelwagon, H. W.: A Treatise on Diseases of the Skin for Advanced Students and Practitioners, ed. 9, Philadelphia, W. B. Saunders Company, 1923.

13. Gottheil: Verrucae Seniles? (Case Presentation), J. Cutan. Dis. **31**:666, 1913.

14. Darier, J.: Précis de dermatologie, ed. 4, Paris, Masson & Cie, 1928.

15. Jadassohn, J.: Die benignen Epitheliome, Arch. f. Dermat. u. Syph. **117**:705, 1914.

16. Wolff: Demonstratem eines Falles von Acanthosis nigricans (Dystrophie papillaire et pigmentaire), Arch. f. Dermat. u. Syph. **47**:417, 1899.

The verrucous lesions had appeared at the age of 5, first on the nuchal region and then in the axillas, afterward becoming generalized. The patient was later shown, at the age of 49, by Pautrier and Hugel [17] and Pautrier and Levy,[18] with microscopic sections of the tumors. The histological picture was that of both the sessile and pedunculated types of seborrheic keratosis. The patient had also acquired squamous cell carcinoma of the groin.

MICROSCOPIC CLASSIFICATION

Montgomery and Dörffel [19] divided seborrheic keratoses into nevoid and verrucous categories, the classification depending on whether the tumors had little or much stratum corneum. They divided the nevoid groups into solid and reticular varieties, with transitions between the two types. Sachs, MacKee and Sachs [20] illustrated only the verrucous type and suggested that the thin lesions be called "seborrheic keratosis" and the thick ones "seborrheic verruca."

ETIOLOGY

Most writers have evaded the issue of causation by including seborrheic keratosis in a chapter on warts and then discussing the cause of warts in general without mentioning the seborrheic variety in particular. The growths have usually been classed with nevi, as by Unna,[8] Pinkus,[21] Darier,[14] Ormsby and Montgomery [2] and others. Unna [8] stated that they differ from pigmented nevi only by their greater fat content. It is now recognized that they do not contain nevus cells and hence are distinct from pigmented nevi. Neumann [6] attributed them to senile changes in the skin. Sabouraud [22] attributed the lesions to localized seborrhea and thought that they were infectious. Jadassohn [15] was of the belief that the disorder is infectious but was unable to prove it. Sutton and Sutton [23] stated that the lesions are evidently autoinoculable. After studying several hundred specimens, I expressed the opinion [24] that the tumors satisfy the requirements for designation as benign epidermal neoplasms. Fischer [25] believed that they are caused

17. Pautrier, L. M., and Hugel: Maladie naevique generalisée à type de dystrophie papillaire et pigmentaire (acanthosis nigricans) et de naevi pigmentaire et verruqueux disseminés sur tout le corps, Bull. Soc. franç. de dermat. et syph. **29**:81, 1922.

18. Pautrier, L. M., and Levy, G.: Maladie pseudo-naevique generalisée à type de dystrophie papillaire et pigmentaire (nouveau type d'acanthosis nigricans anormal), Congrès des dermatologistes et syphilographes de langue française (Strasbourg, 1923), Paris, Masson & Cie, 1925, p. 386.

19. Montgomery, H., and Dörffel, J.: Verruca senilis und Keratoma senile, Arch. f. Dermat. u. Syph. **166**:286, 1932.

20. Sachs, W.; MacKee, G. M., and Sachs, P. M.: Keratosis (Seborrheic and Senile), Arch. Dermat. & Syph. **59**:179 (Feb.) 1949.

21. Pinkus, F.: Haut- und Geschlechtskrankheiten, Leipzig, Klinkhardt, 1910, cited by Freudenthal and Spitzer.[4]

22. Sabouraud, R.: Maladies du cuir chevelu: I. Les maladies séborrhéiques. Seborrhée, acnés, calvitie, Paris, Masson & Cie, 1902. Elementary Manual of Regional Topographical Dermatology, translated by C. F. Marshall, New York, Rebman Co., 1906.

23. Sutton, R. L., and Sutton, R. L., Jr.: Diseases of the Skin, ed. 10, St. Louis, C. V. Mosby Company, 1939.

24. Becker, S. W.: Benign Epidermal Neoplasms, Arch. Dermat. & Syph. **26**:838 (Nov.) 1932.

25. Fischer: Zur Frage des Ausscheidungsdermatosen, Zentralbl. f. Haut- u. Geschlechtsk. **23**:339, 1927.

by altered products of secretion of the cutaneous glands. He also stated that mice painted with scarlet red dye or tar acquire similar tumors. That such tumors also occur spontaneously in mice was evident from my unpublished study of several hundred cutaneous sections of Dr. Maud Slye's mice. In addition to many with true carcinoma, others showed benign epidermal neoplasms similar to seborrheic keratoses.

PATHOGENESIS

Seborrheic keratosis, in its most primitive form, seems to be produced by thickening of the epidermis. The constituent cells resemble basal cells in that they are connected by primitive intercelluar bridges [24] rather than by prickles, as seen in an acanthoma. The surface may be thrown into regularly distributed folds (serrated variety) with elongation of papillae. Thickening of the stratum corneum may be more apparent than real, since soap and water scrubbing goes a long way toward eliminating it. The solid variety shows little or no surface hyperkeratosis, although the protected invaginations and cystlike structures may show a very thick but loose stratum corneum. This observation suggests that surface friction has prevented accumulation of the cornified layer. Parakeratotic epithelium tends to adhere more tenaciously. As the lesion becomes thicker, the picture varies, its features depending on whether the epithelial strands are thick (solid variety) or thin (reticular variety). The papillae are thin or thick, respectively, the opposite of the epidermal strands. The tumor grows outward and does not penetrate as cutaneous carcinoma does.

MALIGNANT NEOPLASIA

Anaplasia is seen in a certain percentage of seborrheic keratoses. Such a change is seen most frequently in tumors showing parakeratosis and is presumed to have resulted from irritation. The involved areas appear more acanthotic than does a quiescent tumor. The changes resemble those seen in a senile keratosis and induced Sutton and Sutton [23] to call such tumors "squamous cell keratoses," from which they maintain that squamous cell carcinoma may result. Sachs, MacKee and Sachs [20] maintain that malignant changes develop in a small percentage of all types of seborrheic keratoses.

Several carcinomas have originated in close proximity to seborrheic keratoses, even if not from the benign tumors themselves. Waelsch's [26] illustrations and those of Eller and Ryan [27] were not as convincing as some others. Pinkus [28] reported the case of a woman, aged 74, with pseudocystic basal cell carcinoma arising in close proximity to a seborrheic keratosis. His illustration shows undoubted carcinoma. Sibley and Muende [29] reported superficial basal cell carcinoma on the chest, along with many seborrheic keratoses. In the discussion,

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26. Waelsch, L.: Über die Verruca senilis und die aus ihnen entstehenden Epithelioma, Arch. f. Dermat. u. Syph. **76**:31, 1905.

27. Eller, J. J., and Ryan, V. J.: Senile Keratoses and Seborrheic Keratoses: Differences Clinically, Histologically and in Susceptibility to Malignant Change, Arch. Dermat. & Syph. **22**:1043 (Dec.) 1930.

28. Pinkus, H.: Über einen Fall von Basalzellenepitheliom auf Verruca senilis, Arch. f. Dermat. u. Syph. **169**:58, 1933.

29. Sibley, K., and Muende, I. K.: Seborrheic Verrucae and Multiple Basal-Celled Epitheliomata, Proc. Roy. Soc. Med. **25**:670 and 926, 1932.

MacCormac and Adamson stated that they did not believe that the tumor itself originated in a seborrheic keratosis, but Muende reported later that tumor cells arose from several inner extremities of the rete processes of a seborrheic keratosis. Montgomery and Dörffel [19] reported the case of an elderly woman with a tumor in the inguinal region. Microscopically the lesion showed both basal cell carcinoma and seborrheic keratosis. Dr. Hamilton Montgomery kindly showed me a section which included a typical squamous cell carcinoma within a seborrheic keratosis. I also had the opportunity, in the summer of 1930, to examine sections of the squamous cell carcinoma in the case of Pautrier and Levy [18] at the Dermatological

TABLE 2.—*Microscopic Diagnosis in 184 Cases in Which the Clinical Diagnosis Was Seborrheic Keratosis*

	No.	Per Cent
Seborrheic keratosis	152	82.0
Carcinoma	8	4.4
Keratosis	4	2.2
Nevus pigmentosus	3	1.6
Verruca vulgaris	3	1.6
Collagen degeneration	2	1.1
Lupus erythematosus	2	1.1
Dermatitis	2	1.1
Thrombosed hemangioma, condyloma acuminatum, adenoma sebaceum, Bowen's disease, lentigo, verruca plana, keratotic nevus and acanthoma, each	1	5.0

TABLE 3.—*Clinical Diagnosis on 234 Lesions on Which Microscopic Diagnosis Was Seborrheic Keratosis*

	No.	Per Cent
Seborrheic keratosis	152	65.0
Nevus pigmentosus	29	12.0
Verruca vulgaris	18	8.0
Senile keratosis	10	4.0
Carcinoma	10	4.0
Granuloma pyogenicum	3	1.0
Lentigo maligna and melanoma	3	1.0
Fibroma	3	1.0
Adenoma sebaceum	2	1.0
Psoriasis, foreign body tumor, tumor and papule, each	1	3.0

Clinic of the University of Strasbourg. The tumor was at least contiguous to a seborrheic keratosis. Freudenthal [30] reported finding a combination of seborrheic keratosis and Bowen's disease in the same tumor in a 70 year old woman.

MATERIAL FOR STUDY

Clinical and/or microscopic diagnosis of seborrheic keratosis was made on 263 specimens from 252 patients in the Dermatological Laboratory of the University of Chicago from Jan. 1, 1949, to April 15, 1950. The so-called cutaneous tags (papilloepithelioma) were not included. Clinical diagnosis of seborrheic keratosis was made on 184 specimens. Laboratory diagnoses on these specimens are given in table 2. Microscopic diagnosis of seborrheic keratosis was made in 234 instances. Clinical diagnoses are given in table 3.

30. Freudenthal, W.: Rumpfhautepitheliom (nebst Bemerkungen über die Verruca senilis und das Keratoma senile), Arch. f. Dermat. u. Syph. **158**:538, 1929.

MICROSCOPIC EXAMINATION

In practically all instances only a single microscopic slide containing several contiguous sections was available. A striking feature of the microscopic picture was the patchy distribution of the various alterations. Signs of inflammation, such as edema, cellular infiltration, crusting and parakeratosis, varied throughout the sections. Surface invagination and pseudocyst formation, hyperkeratosis, hypogranulosis and hypergranulosis showed a spotty distribution. Hypergranulosis alternated with hypogranulosis and parakeratosis. The degree of hyperpigmentation varied in different parts of the sections. The various observations, therefore, do not signify uniformity in a given specimen.

Of the 234 seborrheic keratoses, 211 were sessile and 23 were pedunculated. The epidermal portion of the section, attached stratum corneum being disregarded,

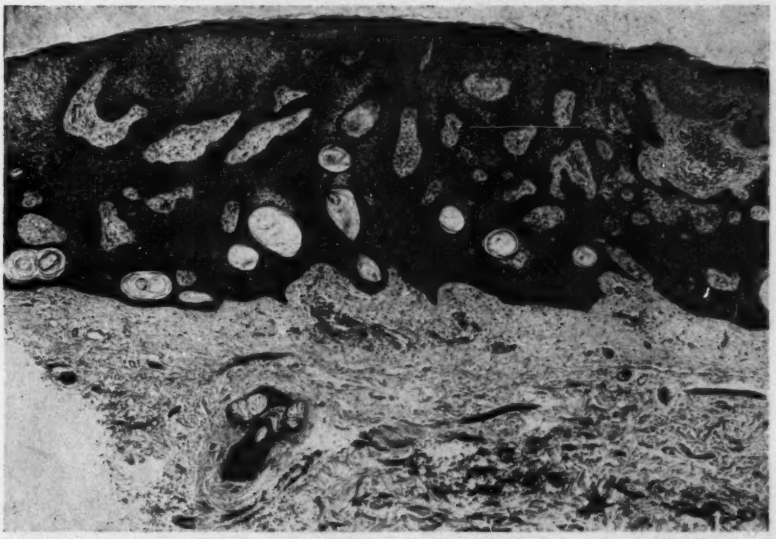

Fig. 1.—Solid type of seborrheic keratosis. The solid epithelial mass is penetrated by narrow papillae and pseudocysts; hematoxylin and eosin stain, × 56.

was measured at its thickest portion. The thickness varied from 0.3 to 3.6 mm. Morphologically, sections were classified as solid (fig. 1), retiform (fig. 2) or serrated (fig. 3). Of the 151 specimens with epithelial portions varying from 0.3 to 0.9 mm. in thickness, 77 were solid, 48 retiform and 26 serrated. Of the 83 specimens with epithelial portions varying from 1.0 to 3.6 mm. in thickness, 51 were solid, 29 retiform and only three serrated. Patchy epidermal edema was present in those portions involved in pronounced inflammation. The stratum granulosum was prominent in at least certain areas of 214 specimens.

Parakeratosis was found in 100 specimens. It was most prominent on exposed surfaces and only occasionally observed in surface invaginations and pseudocysts. Parakeratosis was interpreted as having been a feature of inflammation. This observation closely parallels the phenomenon of anaplasia, seen in 95 specimens.

Fig. 2.—Retiform type of seborrheic keratosis (same patient as in figure 1). Epithelial strands are narrower and the papillae larger; hematoxylin and eosin stain, × 56.

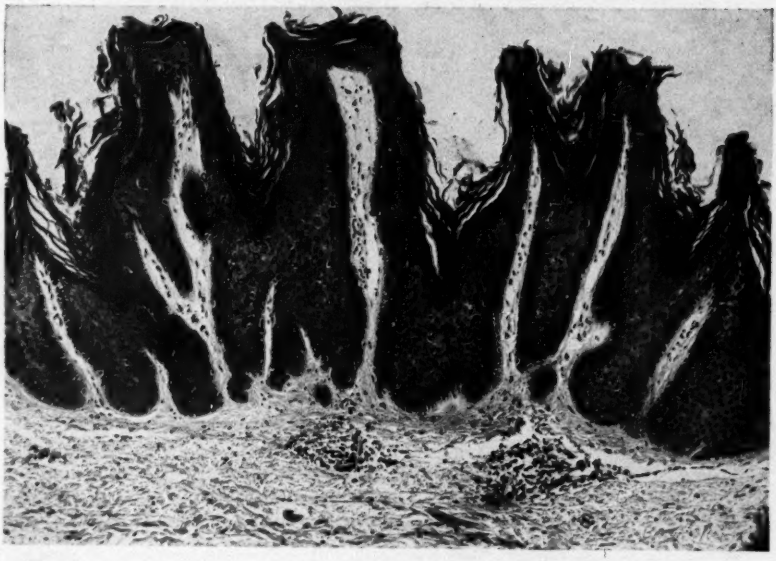

Fig. 3.—Serrated type of seborrheic keratosis; hematoxylin and eosin stain, × 100.

The latter has been described by Montgomery and Dörffel,[19] Sutton and Sutton [23] and others and consisted chiefly in alteration of cell polarity and irregularity in nuclear size and shape and more rarely in individual cell keratinization. Mitotic figures were infrequent, and atypical mitotic figures as seen in true carcinoma were not observed. Crusting was noted in 36 specimens. The sebaceous glands seen in the sections showed, almost without exception, adenomatous changes of the type seen in elderly seborrheic persons. Syringoma was seen in one specimen, and a pigmented nevus was observed in one instance, both conditions in association with seborrheic keratosis.

In 33 specimens, mostly of the pedunculated variety, no surface invaginations or pseudocysts were seen.

HYPERPIGMENTATION

As estimated in hematoxylin and eosin preparations, 84 specimens were hyperpigmented. Clear cells (Masson) were prominent in the pigmented portions. However, it has been shown by Lennox [31] that hyperpigmentation can be demonstrated in 67 per cent of such tumors by a silver method. The disorder is, therefore, a pigmentary dermatosis. I have previously discussed melanotic seborrheic keratosis [32] and have shown that the basal layer is first involved and that the more superficial layers may be involved later. The melanoblasts are normal and show no sign of neoplasia, benign or malignant. In deeply pigmented tumors, melanin-containing chromatophores are seen in the papillae and dermis. The chief significance of deeply pigmented tumors is the fact that the blackest tumors are often mistaken clinically, usually by nondermatologists, for melanoma, as emphasized by Montgomery,[33] and pigmented basal cell carcinoma. They can usually be differentiated by the "pasted-on" appearance of seborrheic keratosis and, of course, by biopsy.

DERMAL INFLAMMATION

Dermal inflammation in varying degree was noted in all specimens. The infiltrate seemed to be of three types. The commonest was a patchy lymphocytic infiltrate in the superficial part of the dermis and some of the papillae, which was considered to be a reaction to deposition of lipids, described by Pollitzer,[10] Kreibich,[34] Carol [35] and others. The more abundant infiltrates contained some plasma cells. The second type consisted chiefly of lymphocytes, occasionally associated with polymorphonuclear leukocytes in some of the superficial papillae, evidently associated with superficial infection or irritation. The third and least common type, seen only in one instance (fig. 4), consisted chiefly of polymorphonuclear leukocytes in the form of an abscess beneath the entire lesion.

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31. Lennox, B.: Pigment Patterns in Epithelial Tumors of the Skin, J. Path. & Bact. **61**:587 (Oct.) 1949.

32. Becker;[24] Cutaneous Melanoma, Arch. Dermat. & Syph. **21**:818 (May) 1930; Melanotic Neoplasms of the Skin, Am. J. Cancer **22**:17 (Sept.) 1934; Dermatological Investigations of Melanin Pigmentation, in Gordon, M., and others: The Biology of Melanomas, New York, New York Academy of Sciences, 1948.

33. Montgomery, H.: Verruca Senilis and Keratoma Senile, Minnesota Med. **18**:735, 1935.

34. Kreibich, C.: Zur Anatomie des Eczema seborrhoicum und der seborrhoischen Warzen, Arch. f. Dermat. u. Syph. **114**:628, 1913.

35. Carol, W. L. L.: Über die Lipiodgehalt der Haut, Dermat. Wchnschr. **63**:834, 1916.

Fig. 4.—Solid seborrheic keratosis with underlying dermal abscess; hematoxylin and eosin stain, × 16.

Fig. 5 (case 1).—Irritated seborrheic keratosis; hematoxylin and eosin stain, × 20.

MALIGNANT NEOPLASIA

Anaplasia of some degree was seen in about 40 per cent of the specimens and was of the same type recorded by Montgomery and Dörffel,[19] Traub and Keil,[36] Sachs, MacKee and Sachs,[20] Sutton and Sutton [23] and others. The following case, reported through the courtesy of Drs. Mercer and McNairy, is illustrative of pronounced anaplasia.

Case 1.—Mrs. J. J. C., aged 55, had had a lesion in the right subscapular area as long as she could remember. Three or four months before observation, and again one month before observation, it had shown signs of irritation and had become tender. Clinically, it was 1.5 by 1.5 cm. and slightly elevated and resembled a basal cell carcinma. Microscopic examination showed that the principal changes occurred in a portion 0.5 cm. long at one end of the tumor (fig. 5). The surface was parakeratotic and crusted (fig. 6). The cellular structure consisted of scattered

Fig. 6 (case 1).—Parakeratotic and crusted seborrheic keratosis; hematoxylin and eosin stain, × 52.

islands of more solid epithelium in a mass of somewhat edematous, anaplastic-appearing cells (fig. 7). The dermal infiltrate was classed as 3 + on a basis of 4.

The section was submitted to Dr. Hamilton Montgomery, who replied as follows: "The section represents, I believe, an early verruca senilis (seborrheic keratosis) which is showing an early intraepidermal epithelioma of Borst-Jadassohn, squamous cell, grade 1. I have seen this phenomenon develop in verruca senilis occasionally in lesions that had been subjected to irritation and trauma, as apparently this one was. It is unusual, of course, to have a verruca senilis develop at birth unless it was dermatosis papulosa nigra in a Negro. A general pathologist simply made a diagnosis of verruca senilis and did not think the lesion was malignant." Diagnosis of "intraepidermal carcinoma or irritated seborrheic keratosis" was made on several similar sections in my series.

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36. Traub, E. F., and Keil, H.: The "Common Mole": Its Clinicopathologic Relations and the Question of Malignant Degeneration, Arch. Dermat. & Syph. **41**:214 (Feb.) 1940.

The only undoubted carcinoma seen in association with seborrheic keratosis during 22 years in our laboratory was that in the following case, reported through the courtesy of Drs. Mercer and McNairy:

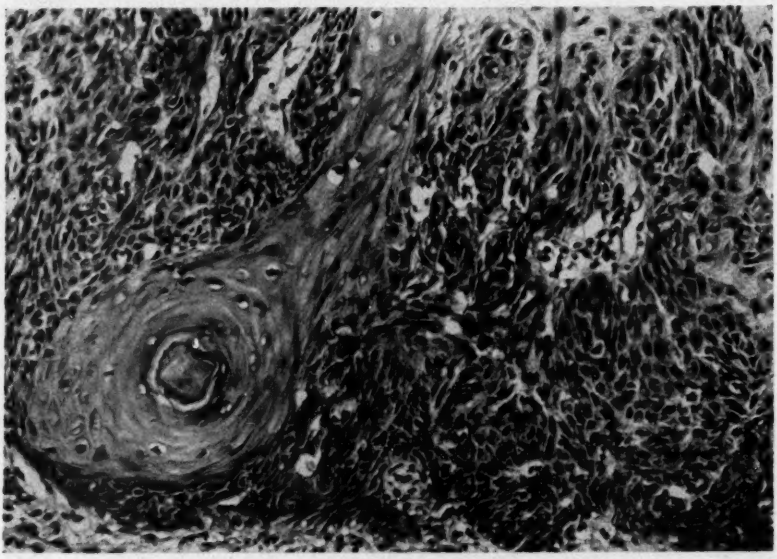

Fig. 7 (case 1).—Anaplastic epithelium in irritated seborrheic keratosis; hematoxylin and eosin stain, × 240.

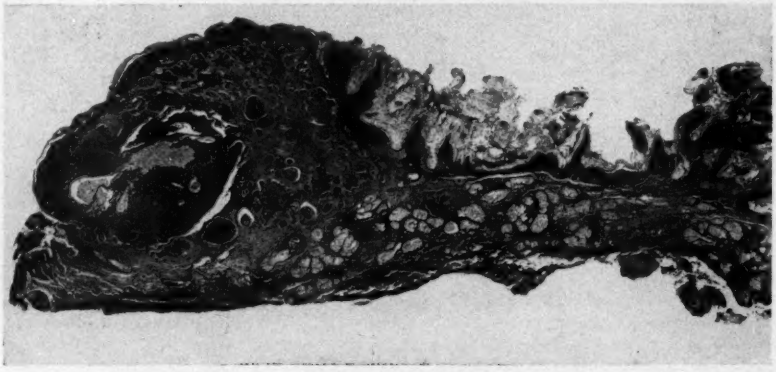

Fig. 8 (case 2).—Seborrheic keratosis and adenoma sebaceum on right and mixed type carcinoma on left; hematoxylin and eosin stain, × 12.

Case 2.—J. L. S., a farmer aged 66, had noted the appearance of a brown lesion near the left inner canthus for 15 years. It had enlarged slowly, but more rapidly in the past four years. Clinically it resembled a pigmented nevus with a central crust.

Microscopic examination (fig. 8) showed typical seborrheic keratosis with underlying adenomatous sebaceous glands. Near one end of the section, where the seborrheic keratosis had thinned out but the epidermis was still hyperpigmented, a carcinoma of the mixed variety was seen to arise from the basal portion of the epidermis. Diagnosis was made of seborrheic keratosis, adenoma sebaceum and mixed type carcinoma. The malignant tumor was at least in close proximity to the benign one, but there is no evidence that the benign tumor cells had given rise to malignant ones.

COMMENT

Diagnosis of seborrheic keratosis may have been made unduly difficult in my series by the large percentage of inflamed lesions. However, careful attention to history and clinical features should result in a satisfactory clinical diagnostic average.

Nomenclature is not entirely praiseworthy, as is shown by the various designations for the disorder (table 1). "Seborrheic keratosis" was formerly used synonymously with "senile keratosis." There is no exact date at which the former term was divorced from the latter. As late as 1920 Williams [37] stated that they are the same, and in 1931 Sutton Sr.[38] emphasized the disagreement among authorities. Some dermatologists, such as Dubreuilh,[39] have always maintained the difference, but Freudenthal,[40] Hookey,[41] Montgomery [33] and others have substantiated the distinction between the seborrheic and senile types. The double designation of "seborrheic keratosis" and "seborrheic verruca" suggested by Sachs, MacKee and Sachs [20] seems to be impractical and unnecessary because of the gradual transition by actual measurement from the thin to the thick lesions.

On the basis of this study, I am more convinced than ever that the tumor is a benign epidermal neoplasm and that the diagnostic term "epithelioma" is the logical one from the pathological viewpoint. Usage is the only support for continued employment of the term "epithelioma" for a malignant tumor. Warthin, and also Robertson,[42] criticized the use of "epithelioma" to designate cancer. The latter, while pathologist at the Mayo Clinic, stated: "Whatever term is used to characterize carcinomas of squamous epithelial surfaces (and I suggest the name I have just used), 'epithelioma' has no place in the nomenclature of tumors and should be dropped." I should like to appeal from Robertson's condemnation and use "epithelioma" for benign neoplasms but not malignant ones. Lennox,[43] whose work on pigmented epithelial tumors has already been mentioned,[31] stated: "Any common benign tumor which never goes malignant is, I think, to some extent suspect as a true neoplasm."

37. Williams, C. M.: Malignant Degeneration in Benign Dermatoses, Arch. Dermat. & Syph. **2**:168 (Aug.) 1920.

38. Sutton, R. L., Sr.: Carcinoma of the Skin, Proc. Staff Meet., Mayo Clin. **6**:357, 1931.

39. (*a*) Dubreuilh, W.: Verrues, in Besnier, E.; Brocq, L., and Jacquet, L.: La Pratique dermatologique. Traité de dermatologie appliquée, Paris, Masson & Cie, 1904; (*b*) Des hyperkeratoses circonscrites, Ann. de dermat. et syph. **7**:1158, 1896.

40. Freudenthal, W.: Verruca senilis und Keratoma senile, Arch. f. Dermat. u. Syph. **152**:505, 1926.

41. Hookey, J. A.: Keratoma Senilis and Verruca Senilis, Arch. Dermat. & Syph. **23**:946 (May) 1931.

42. Robertson, H. E.: The Use and Misuse of Medical Terms: Some Suggestions for Improvement, Proc. Staff Meet., Mayo Clin. **13**:205 (March 30) 1938.

43. Lennox, B.: Personal communication to the author.

Unfortunately, an overwhelming amount of evidence is required to outweigh usage. The combined authority of Virchow, Auspitz and Unna [8] did not avail against the use of the designation "papilloma" for certain benign primarily epithelial growths, and the term is still used by some pathologists for what we call "seborrheic keratosis."

There has been much difference of opinion relative to the development of carcinoma in seborrheic keratosis. According to Beek,[44] one of the reasons for such an assumption is that earlier dermatologists frequently made a clinical diagnosis of carcinoma without microscopic verification. Then, too, the presumed identity of seborrheic and senile keratoses caused prolonged confusion. The frequency of anaplastic changes in my series and the paucity of frank malignancy suggest that such cellular alteration does not lead to true cancer and that it could be better designated as "pseudocarcinomatous anaplasia." My observations are in conformity with those authors, Dubreuilh,[39a] Jadassohn,[15] Pinkus,[28] Montgomery and Dörffel,[19] Darier,[14] Hookey [41] and others, who believe that seborrheic keratosis is not a precancerous disorder.

CONCLUSIONS

In a series of 263 specimens from 252 patients, clinical diagnosis agreed with microscopic diagnosis in 82 per cent or 65 per cent, the figure depending on the method of analysis.

Seborrheic keratosis is not found merely in the aged but has been reported in disseminated form with its onset as early as 5 years of age.

Thickness of the epithelial portion of the tumors varied from 0.3 to 3.6 mm., with such gradual transition that distinction of "seborrheic keratosis" and "seborrheic verruca" does not seen feasible.

The tumor seems to satisfy requirements for diagnosis of benign neoplasm; hence, from a pathological viewpoint, it is best called "epithelioma."

The disorder is not a precancerous one. Anaplasia is a frequent observation in inflamed tumors but is pseudocarcinomatous rather than truly carcinomatous.

Deeply pigmented tumors can be differentiated from melanoma and pigmented basal celled carcinoma only by biopsy. Melanoblasts in the tumors show no sign of neoplasia.

ABSTRACT OF DISCUSSION

DR. FRED D. WEIDMAN, Philadelphia: As usual, Dr. Becker has presented a wealth of material and with an excellent technical study. I shall discuss only two phases of the presentation.

First is that of histological diagnosis. Fortunately, in the great majority of specimens routinely submitted there is not any difficulty. But time and time again there is a problem in respect to basal cell cancer. Thus, occasional examples of these keratoses, instead of extending abruptly upward above the *niveau*, will grow downward and require very fine discrimination for one to decide whether the condition is basal cell cancer or keratosis. Again, I too have encountered a few cases of what Dr. Becker designated as anaplasia—that is, a transformation from the basal type of cell to the squamous. I agree with him that this does not represent a genuine squamous cell cancerous type of change. However, I would not call it anaplasia. I think it is of the order of pseudoepitheliomatous hyperplasia—and, incidentally, two of my cases have been associated with inflammation, which is an acceptable explanation for such pseudoepitheliomatous hyperplasia.

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44. Beek, C. H.: Über die Konstitutions-pathologische Bedeutung der senilen Warzen für die Krebsentstehung, Klin. Wchnschr. **16**:1581 (Nov. 6) 1937.

Second, I shall consider the pathological nature of this dermatosis. Dr. Becker told us of the debate whether the condition was nevoid or neoplastic. In my opinion, these characteristics can be reconciled, much as in the primary epithelial germ tumors. I have been impressed by two features which stand out above all others in stamping seborrheic keratosis with an individuality and which may be significant with regard to pathogenesis.

First, unlike basal cell cancer and many other nevi, the lesion projects abruptly above the surface; this characteristic is almost invariably found with keratoses which have advanced to their full state of development. The next point is that there is consistently (in the fully developed and fully representative lesion) an involved, tortuous, screwy patterning for the papillae. These two features, since they occur so regularly, are at variance with the picture in a neoplasm, such as papilloma. I can see an explanation on the basis that there is an attempt at reproduction of some normal, probably vestigial structure. Just as in neoplasms (including primary epithelial germ tumors) there is an attempt to reproduce some original type of tissue (or even organ), I think that in these keratoses there is an organoid structure, and I would suggest the projecting surface and the screwy patterning of the papillae as pointing toward some specific organ. I would suggest a cutaneous ornament of some kind, such as appears on prehistoric monsters and crocodiles; that is, there may be advanced a phylogenetic explanation comparable to the one which Laidlaw has advanced for other pigmented nevi, in which he suggests a tactile organ (including hairs) as the vestigial organ in the case.

Dr. Charles C. Dennie, Kansas City, Mo.: Many of the invasive lesions that occur on the skin are diagnosed as malignant, especially the pigmented seborrheic keratotic lesions which are solid, round and black and are filled with tiny pores. These characteristics differentiate them from the melanotic lesion, which has no little dents in the top as does the seborrheic keratosis, and make it entirely safe to remove them with surgery or cautery.

Dr. Marcus R. Caro, Chicago: In his many investigations concerning pigmented lesions of the skin Dr. Becker has done much to clarify our knowledge of an obscure yet very important problem. His present contribution, which is based on the examination of a large number of specimens of seborrheic keratoses, shows his usual high degree of painstaking study and tempered judgment.

From my own experience with these tumors I agree that they are not precancerous. The great activity of the cells and the apparent anaplasia often seen in sections may be the result of inflammatory changes. The resemblance to malignant changes may also in some cases be produced by the manner in which the section is cut, exposing the flat plane of the epithelial cells that line the cornified cystlike masses.

To me the greatest importance of pigmented seborrheic keratoses is their occasional resemblance to malignant melanoma. I recently examined a white woman aged 78 years, who had had a dark mole on her abdomen since childhood. The mole suddenly began to enlarge about a year ago. When I saw it the lesion was a walnut-sized, dark bluish black, soft nodule arising from an inflamed base. The clinical picture was so unmistakable that I made the diagnosis of malignant melanoma without any mental reservations and referred the patient to a surgeon for wide excision of the lesion. I was totally unprepared for my histopathological diagnosis of the specimen, which turned out to be pigmented seborrheic keratosis.

I should like to add my plea to Dr. Becker's that more biopsies be performed in cases of tumors of the skin. I can assure you from my own experience that when one performs biopsies in all cases of skin tumors, one's percentage of correct clinical diagnoses will show an unexpected initial drop.

Dr. Stephen Rothman, Chicago: Dr. Becker has emphasized that seborrheic keratoses consist of proliferating basal cells whereas common warts represent true acanthosis or hyperplasia of the rete. Microenzymatic studies confirm these histological observations. Dr. VanScott at the Dermatology Department of the University of Chicago has shown that the arginase activity of the epidermis is tremendously increased in lesions with hyperplasia of the rete, such as psoriasis and common warts, wheras lesions with basal cell proliferation, such as seborrheic keratosis and basal cell carcinomas, do not show any increase of arginase activity.

Dr. Francis A. Ellis, Baltimore: I hesitate to discuss a paper that has been presented by such a master and discussed by such competent men, but there are several points I should

like to stress, Dr. Montgomery is definitely against calling these lesions seborrheic keratoses. I prefer to follow Freudenthal's nomenclature, calling the tumors of this particular group senile verrucas, senile keratoses being placed in another category. Montgomery stresses the fact that senile verrucas are not associated with seborrhea. The color of the lesions before they become hyperpigmented may suggest seborrhea.

Why do many of the cells in these tumors have vacuolization around the nuclei? Is it due to the fact that there is poor nutrition, or it is nevoid? The word "nevoid" is used in a dermatological sense and not as the general pathologist uses it, applying it only to moles.

Dr. S. William Becker, Chicago: I appreciate the interest in such a common and relatively insignificant tumor. In reply to Dr. Weidman, I found one of the greatest aids in differentiating these tumors, which do rarely penetrate rather than grow upward, is the hyperpigmentation of the epithelium. His idea of ornamentation is an excellent one. If I write another paper, I shall be glad to include that idea. Dr. Dennie made some very fine suggestions with which I agree heartily. I agree with Dr. Caro. I am glad to hear Dr. Rothman's microchemical support of the concept of the basal cell origin of the tumors.

In reply to Dr. Ellis, these tumors were called seborrheic keratoses because some of the earlier workers found a certain amount of the fat content in the epithelium and in the dermis, and the presence of lipids accounts, I think, for some of the infiltration which is present in all the tumors. I do not know what would cause the vacuolization. Occasionally we do see a lot of edema in the tumors.

In regard to the terminology, I don't expect to see the name changed to epithelioma in my lifetime. Some 75 or 80 years ago Virchow stated that tumors of the skin which were epithelial should not be called papilloma. Auspitz and Unna echoed this same idea. I added my nickel's worth in 1932, but the tumors are still called papilloma. I think one ought at least to have a term that everybody understands.

Clinical Notes

POLYTHIONIC ACID IN THE THERAPY OF ACNE VULGARIS AND SEBORRHEIC DERMATITIS

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AND
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ACNE

The multiplicity of therapeutic measures suggested for acne vulgaris, the commonest cutaneous disease of adolescence, indicates the lack of specificity of any of them. Sulfur, however, is apparently the most effective local remedy.[1] Drying of the skin, some exfoliation and antiseptic action are expected from the use of sulfur preparations.

The etiology of acne is not clear. Heredity,[2] endocrine disturbances, particularly of the thyroid and pituitary glands,[3] digestive disturbances,[4] disturbances in the water balance,[5] higher activity of the parasympathetic nervous system,[6] and excessive intake of fat [7] and carbohydrates are factors most commonly reported as possibly bearing on the etiology of acne. However, there is much evidence that the last mentioned does not play an important role.[8]

In view of the prominent position occupied by sulfur in the therapy of acne, a preparation of sulfur known as dermasulf® (polythionic acid preparation)[9] was utilized in the treatment of a number of patients with acne and the results compared with those obtained from a different form of sulfur preparation now on the market.

Dermasulf® is a stabilized solution of complex polythionic acids of the general formula $H_2S_xO_6$. The product is without noticeable odor or color. The bulk of the sulfur present is in the form of the tetrathionate or pentathionate. Since the polythionates are water soluble they penetrate the skin more easily and to a greater extent than elemental sulfur, no matter how finely dispersed. Sulfur in this form is more effective than in the polysulfides, which are easily

1. Reque, P. G.: The Practical Management of Acne, J. M. A. Alabama **18**:247-249 (March) 1949.

2. Stokes, J. H., and King, A. D.: Acne Vulgaris: Heredity in Etiologic Background, Arch. Dermat. & Syph. **26**:456-462 (Sept.) 1932.

3. Cohen, E. L.: Endocrine Factors in Acne Vulgaris, Brit. J. Dermat. **53**:231 (Aug.-Sept.); *269* (Oct.) 1941.

4. Whitfield, A.: Some Notes on Acne Vulgaris, Brit. J. Dermat. **46**:257-266 (June) 1934.

5. Stokes, J. H.; Beerman, H., and Ingraham, N. R., Jr.: Carbohydrates and Water Metabolism and Vitamins in Skin Inflammation (Dermatitis), Am. J. M. Sc. **195**:562-574 (April) 1938.

6. Bregman, A.: New Conceptions of Etiology and Pathogenesis of Acne Vulgaris, Arch. Dermat. & Syph. **36**:758-759 (Oct.) 1937.

7. Sutton, R. L., Jr.: Acne Vulgaris, Pustular Lipoidosis: Successful Treatment Based on Control of Lipoid Metabolism of Low Fat Diet and Thyroid Extract, South. M. J. **34**:1071-1082 (Oct.) 1941.

8. Crawford, G. M., and Swartz, J. H.: Acne and the Carbohydrates: Preliminary Report, Arch. Dermat. & Syph. **33**:1035-1041 (June) 1936.

9. Supplies of dermasulf® were furnished through the courtesy of Carroll Dunham Smith Pharmacal Co., New Brunswick, N. J. The preparation is sold in 2.5 and 5 per cent strengths.

oxidized, precipitating elemental sulfur. The polythionate solution presumably delivers the complex sulfur solutions within the affected skin.

Method of Administration.—The patients were given the polythionate preparation and instructed to apply it to the affected skin areas at night before retiring and then allow it to dry. In most cases dermasulf® was recommended for use in the morning as well as at night.

In view of the fact that local applications are usually combined with other forms of therapy in acne, some of the patients treated with dermasulf® were also given vitamin A orally, injections of acne vaccine and/or roentgen therapy. The patients were under treatment from two to six months, with an average of better than three months.

Results.—The results of the treatment are shown in table 1. Table 2 shows the results with another type of sulfur preparation, a stable solution of polythionates of sodium containing sulfur, 1.5 per cent, with zinc oxide, 3 per cent, suspended in distilled water. The duration of treatment with the second type was approximately the same as that with dermasulf.®

TABLE 1.—*Results of the Use of Dermasulf® in Acne Vulgaris*

	No. of Patients Treated	Condition Benefited	No Change	Condition Made Worse	Irritation *	Dose Diminished	Use Stopped
Dermasulf® without other therapy (majority of patients started on solution of 5% strength)	20	10	9	1	8	2	8
5% dermasulf® with other therapy †	61	41	20	0	15	13	12
2½% dermasulf® with other therapy †	55	35	20	0	5	1	7
3¾% dermasulf® with other therapy †	5	4	1	0	1	0	1
Totals	141	90	50	1	29	16	28
Per cent	..	64	35	1	21	11	20

* All irritation was reported, however slight.
† Other therapy consisted in the administration of vitamin A, acne vaccine and/or roentgen therapy.

TABLE 2.—*Results of the Use of a Polythionate with Other Therapy in Acne Vulgaris (Control Study)*

	No. of Patients Treated	Condition Benefited	No Change	Condition Made Worse	Irritation *	Dose Diminished	Use Stopped
Polythionate with other therapy †	50	29	21	0	5	3	6
Per cent	..	58	42	0	10	6	12

* All irritation was reported, however slight.
† Other therapy consisted in the administration of vitamin A, acne vaccine and/or roentgen therapy.

In those patients in whom irritation was produced by the 5 per cent solution the strength was reduced to 2.5 per cent, whereupon the irritation was greatly reduced. In those cases in which irritation from the preparation was excessive this form of therapy was discontinued. It should be borne in mind, however, that some dermatologists believe that mild desquamation from local preparations is desirable in the treatment of acne.

Summary.—1. Of 141 patients treated, 90 were benefited while 50 remained the same and one became worse. Treatment was stopped in 28 cases, either because of lack of benefit or because of irritation.

2. Therapy was well tolerated in the majority of instances. There was no disagreeable odor or color or any visible deposit left on the skin.

3. In conclusion, dermasulf® offers a valuable agent in the therapy of acne, as good as, if not better than, other available preparations of a similar nature.

SEBORRHEIC DERMATITIS

The etiology of seborrheic dermatitis also has not been definitely determined. Recent investigations tend to raise doubt as to older theories regarding infection as the cause. Other possible

causes are endocrine disturbances and dietary errors. Vitamin deficiency also has been suggested.[10]

Dermasulf® was employed in the treatment of the chronic and more resistant forms of seborrhea of the scalp, as well as for seborrheic dermatitis of areas other than the scalp.

Method of Treatment.—For seborrhea of the scalp the patients were instructed to apply the dermasulf® preparation every other night, using a medicine dropper, in fairly small amounts of not more than 20 to 40 drops, the amount used depending on the extent of the area involved, so that the scalp was wetted with the preparation. This procedure was followed by light massage. The patients were under treatment also from two to six months, for an average of about three months.

In some instances it was noted that the preparation had a mild drying effect on the hair. Patients for whom it had this effect found it advantageous to use an oily hair dressing in conjunction with the treatment.

In cases of seborrheic dermatitis of areas other than the scalp the manner and duration of treatment were the same as in the acne cases.

Results.—The results are shown in table 3. It is to be noted that dermasulf® was better tolerated when it was employed on the scalp than when it was applied on other areas of the body.

TABLE 3.—*Results of the Use of Dermasulf® in Seborrheic Dermatitis*

	No. of Patients Treated	Condition Benefited	No Change	Condition Made Worse	Irritation *	Dose Diminished	Use Stopped
Seborrhea of the scalp (majority of patients used solution of 5% strength).	92	67	25	0	3	1	19
Seborrhea other than on the scalp (majority of patients used solution of 5% strength)	20	13	7	0	3	1	5
Totals	112	80	32	0	6	2	24
Per cent	..	71	29	0	5	2	21

* All irritation was reported, however slight.

Since ointments and lotions as a rule are used conjointly in the treatment of seborrhea of the scalp, it was difficult to compare the results obtained from the use of dermasulf® with those from treatment with other preparations.

Summary.—1. Ninety-two patients with seborrheic dermatitis of the scalp were followed in this study. Sixty-seven were benefited, and 25 remained the same, while none became worse as a result of the application of dermasulf.® Its use was stopped in 19 cases because of no benefit or because of irritation.

2. Twenty cases of seborrheic dermatitis of areas other than the scalp were treated with dermasulf.® Thirteen were benefited; 7 remained the same, and none became worse. This form of treatment was stopped in five cases, either because no benefit resulted or because there was irritation.

3. Dermasulf® did not discolor the hair or scalp of any of the patients for whom it was prescribed, but it was tried in the cases of patients with white hair because frequently such preparations cause staining of white hair.

4. Simplicity of usage is a recommendation for the use of dermasulf® in the treatment of seborrheic dermatitis.

5. In conclusion, dermasulf® offers a form of medication for seborrheic dermatitis which is as good as, or better than, any other single preparation which we have used.

55 East Washington Street (2).

10. Ball, F. I.: Dermatitis Seborrheica and Its Management, Ann. West. Med. & Surg. 1:346-350 (Oct.) 1947.

ORAL LESIONS IN PITYRIASIS ROSEA

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Only a single textbook on skin diseases mentions the appearance of mucous membrane lesions in cases of pityriasis rosea. Andrews' textbook [1] mentions that Hazen and Wile have observed such lesions. In 1938 Guequierre [2] presented a case before the Philadelphia Dermatological Society in which there was typical pityriasis rosea with lesions in the mouth. The connection between the pityriasis rosea and the oral lesions was questioned at that time. Guequierre and Wright [3] published a summary of 14 cases of pityriasis rosea with oral lesions in 1941; punctate hemorrhagic lesions were observed in their third case. S. S. Greenbaum [4] reported four cases similar to this third case shortly thereafter. M. J. Costello [5] presented another similar case before the Metropolitan Dermatological Society in 1946; the participants in the discussion emphasized that this was the first case of pityriasis rosea in which they had seen lesions of the mucous membranes. J. Vass [6] mentioned that she had seen mucous membrane lesions in only one out of 270 cases of pityriasis rosea.

Since the appearance of the paper by Guequierre and Wright, I have regularly searched for lesions in the oral cavities in more than 300 cases of pityriasis rosea.

REPORT OF A CASE

J. B., aged 28, was first seen on Dec. 25, 1949.[7] Three days previously he had visited the medical department because of general malaise, constipation and a bitter taste in the mouth. He was sent to the dermatological department because he had skin lesions. His previous history was noncontributory. At the age of 23 he had had chickenpox. The patient did not know how long his eruption had been present. (I should like to remark here that his wife, C. B., aged 23, started treatment at the same time for herpes labialis, which she had had approximately four times yearly since childhood.)

Inspection of the skin showed an eruption distributed symmetrically over the trunk, with emphasis on the lateral areas of the thorax, the shoulders and upper arms, the abdomen and the inguinal region. This eruption consisted of relatively few, discrete pink to salmon red lesions, which had a central, finely wrinkled scale. In some lesions this central scale had dropped off, leaving only a slight peripheral collarette. The lesions, round on the shoulders and oval on the abdomen and back, were so inclined that their longitudinal axis corresponded to the lines of cleavage of the skin. The eruption was more prominent in the inguinal region, and here some of the lesions were confluent. There was some irritation of the lesions in this area, and it was impossible to determine whether or not there had been a herald patch here previously. There was a large amount of seborrheic crusting in the scalp; the patient stated that this condition was of short duration and had begun as a single crusted plaque.

From the Department of Dermatology, the Workers' Sick Foundation, service of Dr. Michael G. Rosenbaum.

1. Andrews, G. C.: Diseases of the Skin for Practitioners and Students, ed. 2, Philadelphia, W. B. Saunders Company, 1938, p. 221.

2. Guequierre, J. P.: Pityriasis Rosea Associated with Oral Lesions. Arch. Dermat. & Syph. **38**:159 (July) 1938.

3. Guequierre, J. P., and Wright: Pityriasis Rosea with Lesions on Mucous Membranes, Arch. Dermat. & Syph. **43**:1000 (June) 1941.

4. Greenbaum, S. S.: Oral Lesions in Pityriasis Rosea, Arch. Dermat. & Syph. **44**:55 (July) 1941.

5. Costello, M. J.: Pityriasis Rosea Associated with Oral Lesions in a Child, Arch. Dermat. & Syph. **53**:73 (Jan.) 1946.

6. Vass, J.: Treatment of Pityriasis Rosea with Nonspecific Substances, Arch Dermat. & Syph. **58**:231 (Aug.) 1948.

7. The patient was presented before the Haifa Dermatological Society on Jan. 4, 1950, by the author, in whose department he was treated.

Inspection of the oral cavity revealed eight to 10 dark red, discrete, pinpoint-sized to pinhead-sized lesions on the soft palate approximately 1 cm. above the base of the uvula.

The results of the routine laboratory tests were within normal limits. The exanthem on the trunk spread; the lesions became confluent and then lost their scale and faded by Jan. 15, 1950. The lesions on the mucous membranes took a different course. Four days after the first examination, two small, sharply circumscribed, hemorrhagic lesions appeared between the previously mentioned pinpoint lesions. These lesions increased in size during the next few days, reaching a maximum diameter of 7 and 5 mm., respectively. The lesions in the mouth rapidly regressed, and on Jan. 10, 1950, (five days before the disappearance of the cutaneous lesions) they were completely healed.

DIFFERENTIAL DIAGNOSIS

A number of diseases were considered in the differential diagnosis. In avitaminosis C, or scurvy, extravasations of blood are found in and beneath the mucous membranes. At the same time, however, bleeding, swollen gums, gingival petechiae and perifollicular hemorrhages on the lower extremities are found. Petechiae and ecchymoses appear in great numbers on the skin and mucous membranes in thrombopenic purpura (morbus maculosus werlhofii). In influenza dark red petechiae are noted on the buccal mucous membrane but usually disappear within one to two days and are only a symptom of the general disease. I recently observed telangiectasia on the skin of the cheeks and numerous discrete hemorrhagic lesions on the back of the tongue in a father and daughter who both had Osler's disease. In severe gonorrhea with gonococcemia, round or oval petechiae on the skin over the joints and on the conjunctiva and mucous membranes may occasionally be seen. These lesions may appear in crops and are usually accompanied with a sudden rise in temperature.

In my case all these possibilities could be ruled out with ease. It is natural, if the mucous membrane lesions are to be connected with the coexisting pityriasis rosea, to regard them as enanthemas of pityriasis rosea. This case is very similar to the third case of Guequierre and Wright, as well as to Greenbaum's cases. In this case, as in Greenbaum's cases, the enanthemas appeared at the height of the disease and regressed before the skin lesions disappeared.

SUMMARY

A case of pityriasis rosea associated with oral lesions is presented.

The differential diagnosis is discussed.

SEX HORMONE SENSITIZATION (CORPUS LUTEUM)

W. H. GUY, M.D.

F. M. JACOB, M.D.

AND

W. B. GUY, M.D.

PITTSBURGH

Since H. Géber [1] in 1921 first demonstrated menstrual urticaria comparatively few case reports have appeared in the literature. In 1930 H. Géber [2] reported successful treatment of the disorder by injections of autoserum of the menstrual epoch. Zondek and Bromberg [3] tested for allergic sensitivity, using steroids in oil. They obtained a high percentage of false positive reactions due to the oil and later avoided this result by giving the injections deeper. Phillips,[4]

From the Department of Dermatology and Syphilology, University of Pittsburgh.

1. Géber, H.: Einege Daten zur Pathologie der Urticaria menstruationalis, Dermat. Ztschr. **32**:143, 1921.

2. Géber, J.: Desensitization in the Treatment of Menstrual Intoxication and Other Allergic Symptoms, Brit. J. Dermat. **51**:265, 1930.

3. Zondek, B., and Bromberg, Y. M.: Endocrine Allergy: Allergic Sensitivity to Endogenous Hormones, J. Allergy **16**:1, 1945.

4. Phillips, E. W.: Clinical Evidence of Sensitivity to Gonadotropins in Allergic Women, Ann. Int. Med. **30**:2:364, 1949.

reporting on two years' experience with water-soluble gonadotropins, found 107 positive reactions to them in allergic women. Attempted desensitization by injections of synapoidin® (a combination of chorionic gonadotropin from human pregnancy urine and follicle-stimulating hormone from anterior pituitary glands, biologically standardized to contain 15 synergy rat units per cubic centimeter) was of doubtful service in three cases of urticaria. In 1948 Baer, Witten and Allen [5] reported testing 165 cases. In 30 cases with a definite clinical relationship to genital function four positive reactions were obtained, and in two cases desensitization was accomplished by injections. In 64 nonrelated cases no reactions were obtained. These authors tested with steroid hormones, estrone, estradiol, progesterone, testosterone, androsterone and desoxycorticosterone. Readings were made after 24 and 48 hours. These studies postulated the existence of sex hormone sensitization, its rarity and its amenability to successful desensitization. The following case report represents the successful application of these principles in diagnosis and treatment of a unique case.

A 28 year old woman consulted us regarding a generalized urticaria of six years' duration. At first the eruption had appeared only at the premenstrual period, but during the previous two years it had been continuous but aggravated during the menstrual epoch. The patient enjoyed good general health except for nervous tension. In the course of a general survey, intradermal tests with 5 per cent aqueous estrone, synapoidin® and extract of corpus luteum were made. Readings made at ½ hour, 24 and 48 hours later revealed a moderate reaction to the first two and a very strong reaction to extract of corpus luteum. Treatment along dietetic lines plus the use of antihistamine drugs, ephedrine and a bromide, charcoal and pepsin elixir mixture was abandoned, and injections of corpus luteum were made at five day intervals, between menstrual periods, beginning with 0.1 cc. and increasing to 0.5 cc. The patient's urticaria gradually improved until she was receiving 0.5 cc. of corpus luteum, at which time she became symptom free. Injections were continued for one month, after which period treatment was discontinued. The patient had remained free of urticaria six months at the time of writing.

7026 Jenkins Arcade (22).

5. Baer, R. L.; Witten, V. H., and Allen, J. R.: Skin Tests with Endocrine Substances: Method of Zondek and Bromberg, Ann. Allergy **6**:239, 1948.

TUBERCULOSIS VERRUCOSA CUTIS TREATED WITH STREPTOMYCIN

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PROVIDENCE, R. I.

Numerous reports have attested to the efficacy of streptomycin in the treatment of cutaneous tuberculosis.[1] However, its beneficial action, for the most part, has been observed only in certain types of involvement, namely cutaneous sinuses and fistulas. A review of the literature discloses only two cases of tuberculosis verrucosa cutis treated with streptomycin. The first was included in a report by Combes, Canizares, Shatin and Kaufman,[1f] and the second was more recently

From the Department of Dermatology and Syphilology of Bellevue Hospital, Dr. Frank C. Combes, chief of service, New York.

1. (*a*) Streptomycin in the Treatment of Infections, Committee on Chemotherapeutics and Other Agents, National Research Council, J. A. M. A. **132**:70 (Sept. 14) 1946. (*b*) O'Leary, P. A.; Ceder, E. T.; Hinshaw, H. C., and Feldman, W. H.:: Treatment of Various Types of Cutaneous Tuberculosis with Promizole and Streptomycin, Arch. Dermat. & Syph. **55**:222 (Feb.) 1947. (*c*) Annual Report of the Committee on Therapy and the Subcommittee on Streptomycin, J. A. M. A. **135**:641 (Nov. 8) 1947. (*d*) Feldman, W. H., and Hinshaw, H. C.: Streptomycin: A Valuable Anti-Tuberculosis Agent, Brit. M. J. **1**:87 (Jan. 17) 1948. (*e*) Tucker, W. B.: Streptomycin in the Treatment of Various Tuberculous Conditions, Journal-Lancet **68**:282 (July) 1948. (*f*) Combes, F. C.; Canizares, O.; Shatin, H., and Kaufman, C.: Streptomycin in Dermatology: Its Value and Limitations, New York State J. Med. **48**:2024 (Sept. 15) 1948. (*g*) Whitehead, H. G.: The Present Status of Streptomycin in the Treatment of Tuberculosis, Bull. School Med. Univ. Maryland **33**:79 (Oct.) 1948.

presented by Allison, Robinson and Frutchey.[2] In both cases 1 Gm. of streptomycin was given daily for six weeks with rapid involution of the lesions. This report concerns a third patient with tuberculosis verrucosa cutis successfully treated with streptomycin.

Fig. 1.—Verrucous and keratotic lesions of the hand prior to treatment with streptomycin.

Fig. 2.—Appearance of the hand after completion of a course of streptomycin. The lesions had disappeared, only a faint erythema indicating the sites of previous involvement.

REPORT OF A CASE

M. C., a 35 year old white woman, gave a history of hoarseness and cough of several months' duration. Roentgenologic studies showed evidence of moderately advanced pulmonary tuberculosis, confirmed by the finding of tubercle bacilli in her sputum. On her left hand were several keratotic, verrucous lesions, surrounded by a very thin zone of erythema, on the fourth and fifth fingers and adjacent dorsal and ulnar surfaces (fig. 1). These had been present for four years

2. Allison, J. R.; Robinson, A. M., and Frutchey, L. D.: Tuberculosis Verrucosa Cutis Successfully Treated with Streptomycin, J. Invest. Dermat. **13**:207 (Oct.) 1949.

and had resisted all topical therapy. A biopsy showed a histological structure characteristic of tuberculosis verrucosa cutis. The patient was given streptomycin in a dosage of 1 Gm. daily for six weeks. Response of the cutaneous lesions was striking; at the end of two months, with the exception of slight residual erythema, there was complete involution (fig. 2). Three months later the erythema itself had disappeared. Despite the dramatic effect on the cutaneous lesions, the streptomycin produced no change in the pulmonary disease, as demonstrated by roentgenograms, and the sputum continued to contain acid-fast bacilli.

COMMENT

Michelson [3] has stated that the treatment of tuberculosis verrucosa cutis should be "by means of roentgen irradiation, application of solid carbon dioxide or excision." The results observed in the case reported and in the other two cited indicate that there is still another mode of therapy for this disease.

One of the serious limitations to the use of streptomycin in the treatment of tuberculosis is the development of resistance of the tubercle bacilli to the drug. It has been pointed out that this may occur as early as the thirty-fifth day when low doses are employed and even sooner when larger doses are used.[4] Development of resistance may make the drug valueless later at the time of spread of the disease. For this reason, not every case of tuberculosis cutis should be treated with streptomycin. If evidence of pulmonary involvement is present, consultation with a phthisiologist concerning the possible effect of treatment on the pulmonary disease is advisable. If it is decided to use streptomycin for the cutaneous lesions, it should be given in daily doses of not greater than 1 Gm. and continued for no longer than five to six weeks in order that the possible development of resistance may be avoided.

SUMMARY

The third case of tuberculosis verrucosa cutis successfully treated with streptomycin is reported.

It is suggested that if there is evidence of tuberculosis elsewhere in the patient consultation with a phthisiologist is advisable before such therapy of the cutaneous lesions is started, and, if given, low doses over a short period should be employed.

ADDENDUM.—Since submission of this report, Johnson's [5] article concerning the successful treatment of three cases of tuberculosis verrucosa cutis with dihydrostreptomycin and potassium iodide has been published.

247 Waterman Street (6).

3. Michelson, H. E., in discussion on Ringrose, E.: Tuberculosis Verrucosa Cutis of the Finger, Arch. Dermat. & Syph. **61**:516 (March) 1950.

4. Whitehead.[1g] Pfuetze, K. H., and Pyle, M. M.: Streptomycin in Tuberculosis, Minnesota Med. **31**:1309 (Dec.) 1948.

5. Johnson, H. M.: Dihydrostreptomycin and Potassium Iodide in the Treatment of Tuberculosis Verrucosa Cutis, J. Invest. Dermat. **15**:61 (July) 1950.

SUBCUTANEOUS INJECTIONS OF PROCAINE PENICILLIN IN TREATMENT OF CHRONIC SYCOSIS VULGARIS AND HIDRADENITIS SUPPURATIVA AXILLARIS

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Sycosis vulgaris, a purulent folliculitis and perifolliculitis of staphylococcic origin, and hidradenitis suppurativa, an inflammatory disease in apocrine gland–bearing areas which is some-

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times referred to as a staphyloderma, have several things in common: the infectious agent, the extreme chronicity and the frequent remissions and relapses. In addition, both these conditions are deep infections, for in chronic sycosis vulgaris [1] the pathological process may involve the entire cutis and in hidradenitis suppurativa [2] the infection usually spreads throughout the subcutaneous tissues. In the later stages of hidradenitis suppurativa suppuration persists and extends into the deep layers of the subcutaneous tissue with the formation of extensive sinus tracts.

The methods of treating these disorders are legion, and the prognosis not always favorable. George C. Andrews [3] in discussing the treatment of hidradenitis suppurativa axillaris advises, first, roentgen therapy as the therapy of choice and, second, in cases in which there is no response to irradiation, surgical excision of the affected skin area and replacement with a full thickness graft. Finally, he states that the administration of estrogenic substances and simple surgical incision, drainage and irrigation of individual abscesses with a solution of penicillin are of little practical value. Ormsby and Montgomery [4] suggest in addition internal administration of sulfathiazole, sulfanilamide and nonspecific proteins. As for the treatment of chronic sycosis, numerous local medications, antibiotics, grenz rays and roentgen rays are employed. These treatments are sometimes very successful, but not infrequently they end in failure or recurrence. Since penicillin became available in large quantities it has been tried in cases of sycosis vulgaris in many forms: sprays, wet compresses, gels, creams, ointments and intramuscular injections, with varying degrees of success. However, this success has usually been only temporary.

Since June 1949 I have used penicillin in hyaluronidase as a form of therapy in eight cases of chronic sycosis vulgaris. All the cases were of four or five years' duration, and the patients had received many forms of treatment without success. In view of good reports on local injections of penicillin in furunculosis, the use of aqueous penicillin G potassium injections subcutaneously in the areas of thickened plaques was attempted; these injections were quickly abandoned because they proved too painful to the patient. A change to procaine penicillin aqueous suspension, 300,000 units per cubic centimeter, was made in the hope that the procedure would prove painless and that the extreme insolubility of the penicillin would provide a concentrated amount of the antibiotic for effective action. These injections were painless, but the technical difficulties caused by blockage of needles by the procaine penicillin crystals while injections were made into indurated areas were sufficiently great to make us discontinue this method. It was hoped that these difficulties might be overcome by use of hyaluronidase enzyme (the so-called spreading factor), which has been successfully used to facilitate absorption in hypodermoclysis. The combination of procaine penicillin (300,000 units per cubic centimeter in hyaluronidase [5] (in doses of from 50,000 to 300,000 units with 250 viscosity units of hyaluronidase powder in 0.5 to 1.0 cc. of sterile distilled water) proved technically very successful. Injections could easily be given subcutaneously into the thickened patches through a 22 gage needle when a freshly prepared mixture was used immediately.

Injections were not given into areas of local discrete follicular infections but only into the chronic plaques. Each chronically involved area was treated separately. The injections were given every two or three weeks, and only from one to four injections were required to get satisfactory results. Clinically the results were remarkable; areas became less indurated or practically normal, the rate of improvement depending on the previous severity of the case. There were no systemic reactions from the combination of procaine penicillin and hyaluronidase. With the administration of the larger amounts of penicillin the infiltrations became slightly tender for several days, and warm wet compresses were used for relief. There were no other local reactions. No spreading of infection which could be attributed to hyaluronidase was

1. Ormsby, O. S., and Montgomery, H.: Diseases of the Skin, ed. 7, Philadelphia, Lea & Febiger, 1948, p. 1386.

2. Ormsby and Montgomery,[1] p. 1276.

3. Andrews, G. C.: Diseases of the Skin for Practitioners and Students, ed. 3, Philadelphia, W. B. Saunders Company, 1946, pp. 790-791.

4. Ormsby and Montgomery, [1] p. 1277.

5. Alidase,® the brand of hyaluronidase used, was supplied for this work by courtesy of G. D. Searle & Co.

encountered. To maintain the benefits obtained and to clear the residual discrete follicular infections quinolor® ointment (benzoyl peroxide, 10 per cent, and chlorhydroxyquinoline, 0.5 per cent, in a base of equal parts of white petrolatum and deodorized wool fat) was used.

Since February 1950 I have treated three patients with chronic hidradenitis suppurativa axillaris of several years' duration with weekly injections of procaine penicillin G for aqueous injection [6] without hyaluronidase (150,000 units per cubic centimeter instead of the previously used 300,000 units per cubic centimeter). The results were very gratifying from the very first treatment. The injections themselves presented no technical difficulties; that is, the procaine penicillin in this dilution did not block a 22 gage needle. The injections were not painful. The resistance of the tissues in the axillas was nominal as compared with the resistance of the tissues in sycosis of the face. There were no complications in the form of painful nodules or sensitivity reactions.

Although penicillin has been used previously in these conditions, both by intramuscular injection and surface application, such procedures have not proved of great worth in chronic pyodermic lesions because they have not reached the involved areas in sufficient concentrations to be of definite therapeutic value. I have chosen the aqueous suspension of procaine penicillin, which can be administered by subcutaneous injection, because of its extreme insolubility, it thus providing a repository form of concentrated penicillin at the site of the infection.

SUMMARY

Subcutaneous injections of procaine penicillin (crysticillin®), 50,000 to 300,000 units, using 150,000 units per cubic centimeter and a 22 gage needle, are offered as a highly useful therapeutic agent in the treatment of such chronic pyodermic infections as sycosis vulgaris and hidradenitis suppurativa.

Eight cases of sycosis vulgaris of the face and three cases of hidradenitis suppurativa axillaris were thus treated with most satisfactory results.

There were no sensitivity reactions either to penicillin or to the procaine component.

Hyaluronidase in amounts of 250 viscosity units was originally used to facilitate the subcutaneous injections of highly concentrated crysticillin (300,000 units per cubic centimeter).

Hyaluronidase with procaine penicillin injected subcutaneously in cases of sycosis vulgaris did not spread infection, as might have been expected.

Subcutaneous injections of procaine penicillin G in an aqueous suspension appear to be equally effective with or without hyaluronidase.

Aqueous suspension of procaine penicillin was chosen for this work because of its extreme insolubility, highly concentrated amounts of the antibiotic thus being allowed to act directly at the site of the infection.

It is hoped that this procedure will be utilized for chronic infections of a similar nature.

6. Crysticillin® (Squibb), the product used, is a dry crystalline procaine penicillin G combined with suitable and harmless dispersing and stabilizing agents. It contains no oil or wax.

Society Transactions

BRONX DERMATOLOGICAL SOCIETY

Charles R. Rein, M.D., *Vice President, in the Chair*

Henry Silver, M.D., *Secretary*

Jan. 19, 1950

Giant Condylomata Acuminata of the Penis Associated with Metastatic Carcinoma of the Right Inguinal Lymph Node. Presented by Dr. Charles F. Sims and Dr. John Garb.

A. B., a Negro aged 72, a painter, registered at the Skin and Cancer Unit of the New York University–Bellevue Medical Center on Jan. 27, 1949, presenting a massive growth, of one year's duration, on the penis. He gives no history of previous serious illnesses, denies venereal infection and appears to be in good general health. About June 1947 a "blister" appeared on the dorsal surface of the shaft of the penis, for which condition he received three injections of penicillin. Six months later there developed a lesion on the same site, which kept growing rapidly.

The patient presents an irregular, cauliflower-like, foul-smelling, erythematous moist growth on the entire shaft of the penis, most pronounced on the left side, measuring 9 cm. in its widest diameter. The penis, except for some portion of the glans, is entirely denuded of epidermis. There are many longitudinal transverse sinuses present throughout the growth. The left inguinal lymph node is enlarged to the size of a bean; the enlarged right inguinal lymph node has been removed for histological study. In the past four months the scrotum has become enlarged to the size of a small grapefruit. The urine is discharged from the posterior surface of the shaft of the penis, the normal urethral opening having become obstructed.

Examination of the urine showed no abnormalities. The serologic tests for syphilis gave positive reactions. The blood serum contained 5.1 Bodansky units per 100 cc. (normal, 3 to 5) of alkaline phosphatase and 2.7 Gutman units per 100 cc. of acid phosphatase (normal, 0.5 to 2.5). The basal metabolic rate was within normal limits.

Intracutaneous tests with Frei antigen and Ducrey vaccine gave a 2+ and a 3+ reaction, respectively. Direct smear examination revealed no Hemophilus ducreyi. The hemogram on April 14, 1949 showed 3,400,000 erythrocytes and 9.3 Gm. of hemoglobin. The leukocyte count was 11,600, with 30 polymorphonuclear leukocytes, 50 lymphocytes, 31 eosinophils and 9 monocytes per hundred cells. The hemogram done on Jan. 11, 1950 showed 3,900,000 erythrocytes and 9.8 Gm. of hemoglobin (66 per cent). The color index was 0.84. There was moderate achromia, slight anisocytosis and polychromasia. The leukocyte count and differential count were normal.

The total protein content in the blood serum was 8.5 Gm. (normal, 4 to 5). The globulin content and albumin-globulin ratio were normal.

Four sections were taken from various parts of the growth between Jan. 27 and April 25, 1949, and examined by Dr. C. F. Sims. The sections showed a decidedly acanthotic epidermis which was thrown into large folds. There were some mitotic figures present. The sections examined on April 14, 1949 showed a pseudoepitheliomatous acanthotic epidermis. The upper part of the cutis was highly edematous, revealing dilated blood vessels and a dense cellular infiltrate composed of numerous plasma cells, polymorphonuclear neutrophils, small round cells and wandering connective tissue cells. The histological diagnosis was condylomata acuminata, with no evidence of malignant changes.

Histological examination of a section taken from the excised right inguinal lymph node on April 6 showed squamous cell carcinoma "secondary to carcinoma of the penis." Smears studied at the Board of Health and at the Skin and Cancer Unit failed to reveal Donovan bodies.

The physical examination revealed no further abnormality. The eyes reacted to light and in accommodation. Rectal examination revealed no stricture. Roentgenograms showed no evidence of metastasis in the pelvis. The lung fields were comparatively clear.

The patient was advised to have surgical ablation of the penis, which he refused.

DISCUSSION

DR. LUDWIG LOWENSTEIN (by invitation): The mere fact that the lymph node shows cancer cells speaks definitely for the diagnosis of cancer of the penis. This case represents a condyloma-like carcinoma belonging to the group described by Freudenthal and Spitzer (Handbuch der Haut und Geschlechtskrankheiten, Berlin, Julius Springer, 1933, vol. 12, pt. 3).

In contrast to this, I should like to call the group of cases which Buschke and I described in 1932 (*Arch. f. Dermat. u. Syph.* **163**:1, 1931) carcinoma-like condyloma. These presented clinical features similar to those of the case presented tonight. However, at no time were there any histological observations of carcinoma, neither on the penis nor in the lymph glands. The essential histological distinction of the Buschke-Lowenstein tumors from simple condyloma is that the former show a pronounced tendency to infiltrate and penetrate into the deeper tissues. This infiltrating growth with destruction of the tissue stroma is certainly a sign of malignancy; that point is what led us to call the tumors carcinoma-like condylomas. We believe, however, that this infiltration is not an active one—that in the Buschke-Lowenstein tumors we are dealing with condyloma tissue which has simply been displaced downward by the prolific growth of condyloma above it. The effect of this process is to compress a portion of the corpus cavernosum. Nowhere are tumor cells to be seen—not in the tissue spaces, the blood vessels or the lymphatics.

Since there is not a single place where tumor cells invaded the blood vessels or lymphatics, no dissemination of tumor cells to the lymph nodes (metastases) could occur. The sharply demarcated epithelial boundary and the absence of so-called "cancer cell nests" and other characteristics for cancer justify regarding the form of tumor we described as relatively benign, particularly as no recurrences have appeared after sufficiently thorough removal. In all cases of this type, it has been repeatedly emphasized that there is no essential deviation from the usual picture of ordinary condyloma acuminatum, especially no disorganization of the epidermal layers and no extensive formation of epithelial pearls. We stressed the sharp and regular demarcation of the epithelial papillae and repeatedly pointed out that the infiltration with leukocytes, lymphocytes and plasma cells is somewhat greater than in ordinary condylomas.

The fact that the condylomata acuminata of the vulva and vagina, in spite of their gigantic proportions, always remain superficial led us to suppose that the downgrowing type of proliferation seen in males is in a certain sense perhaps partly determined by mechanical factors.

DR. JULIUS H. POLLOCK: I should like to suggest the diagnosis of prickle cell epithelioma in a long-standing case of granuloma inguinale. At the Clinic of the Department of Health of the City of New York I have seen many cases of granuloma inguinale of long duration. Some of the patients, especially before the advent of streptomycin, returned years later with large, broken-down fungating masses. Some of the lesions in these stages did not reveal Donovan bodies. Clinically the lesions resembled epithelioma.

Biopsies from these lesions are not often interpreted correctly. Sometimes the pseudo-epitheliomatous changes in the epidermis may be mistaken for malignant ones; at other times "granulation tissue only" is reported when, as a matter of fact, the epithelioma may be present in deeper sections or not at all in the tissue removed. However, I have had patients with authenticated cases of granuloma inguinale of long standing who eventually showed the picture of a malignant growth both clinically and histologically, and there is no reason why such a condition could not eventuate in a long-standing chronic disease such as granuloma inguinale, as it may have done in this case.

The operation, in order to be thorough, requires almost total resection of the penis. Before one resorts to such a radical procedure, especially since there is a question of malignancy, as in this case, the patient should be given the benefit of antimony or streptomycin therapy.

DR. ARTHUR B. HYMAN: Whatever the reason for this situation may have been, there is a missing link here between the pathological picture of the lesion of the penis which showed condyloma acuminatum and the section of the node which showed prickle cell epithelioma, and this lack has thus far not been explained. One must assume that had a deep enough section been taken prickle cell epithelioma would have been found in the penile lesion. Otherwise, the following possibilities are suggested: the patient has condylomata acuminata of the penis, and it is remotely conceivable that there is "metastasis" of benign tissue in the

lymph nodes. But then, of course, one should find tissue like condyloma, not prickle cell epithelioma, in the lymph nodes. Here we have condyloma acuminatum showing only in the penis and prickle cell epithelioma in the lymph node, and we can assume that benign tissue was carried from the penis to the lymph node and that in the lymph node that tissue became malignant. Such a theoretical possibility is hardly acceptable. We must therefore assume that there actually is prickle cell epithelioma in the penis to be found only in deep tissue. This is the only reasonable explanation.

DR. CHARLES WOLF: Before one accepts the diagnosis of two different conditions, one should carefully analyze the process going on here. The possibility that we are dealing with one disease is acceptable. The possibility that we are dealing with two conditions is debatable. For the sake of argument let us assume that the disorder is condyloma acuminatum. It is possible that malignant changes have developed in the tissue as a result of chronic irritation, which is a potent cause of carcinoma. The fact that the biopsy does not bear out any evidence of malignant changes in the penis does not exclude the possibility of their being present. The carcinoma may be at the base of the lesion, not to be found unless the entire lesion is excised and further search is made. In the section there was nothing to suggest prickle cell carcinoma.

DR. MAX JESSNER: When the patient was first seen at the clinic, we thought of epithelioma or of epithelioma-like condyloma acuminatum which may perforate the prepuce, as in the cases described by Buschke and Lowenstein, W. Frei and others. Several biopsies were made and no evidence of epithelioma found. I doubt that one will find epithelioma on further histological study. The situation is, of course, puzzling, but, if after examining four biopsies one does not find carcinoma and the biopsies were made deeply, then one must assume the disorder is not carcinoma but condyloma acuminatum. An excised lymph node was declared by the general pathologist to contain metastatic carcinoma, but the cell nests were sharply defined and the cells were regular and not angry looking. Nevertheless, since the lymph node was invaded we have to regard this case as one showing malignant changes. This would be, to my knowledge, the first case of condyloma acuminatum with metastasis into the lymph node. A good example of virus papilloma that can become malignant and metastasize into the lymph node is the Shope papilloma.

DR. JOHN GARB: I have fully discussed the pathological aspect of this case with Drs. Maurice N. Richter and Charles F. Sims, and the following possibilities were suggested: (1) that the lymph node shows a metastatic carcinoma from the penile growth and that in spite of the absence of carcinomatous cells in the four biopsies there are squamous cell carcinomatous areas in the penile growth which we were not able to get at; (2) that the condition is squamous cell carcinoma of the right inguinal lymph node, metastatic from another unknown source and (3) that it is an epithelial growth in the right inguinal lymph node metastatic from the cells of condylomata acuminata. The latter possibility would be extremely interesting and worth investigating. I feel that, although condylomata acuminata are classed as benign, because of their rapid growth they could perhaps, like a malignant growth, invade the adjacent inguinal lymph nodes.

Further and deeper sections will be taken. Unless we find carcinoma cells in the deeper sections I would rather label this case carcinoma-like condylomas.

Sporotrichosis. Presented by DR. EMANUEL MUSKATBLIT and (by invitation) DR. LOUIS TULIPAN.

J. D., a white man aged 58, struck his left hand while digging a sewer on Feb. 24, 1949. Two days later he noted a swelling of the hand which failed to respond to treatment. Three or four months after the initial injury he noted the progressive appearance of "sores" on the left hand and forearm.

When first seen by us, on Dec. 8, 1949, he presented six discrete raised purulent, discharging abscesses the size of a marble. One was situated on the dorsum of the left middle finger, and the others were distributed in an ascending linear fashion up the forearm with the highest lesion on the level of the midarm. There were no palpable axillary nodes.

A clinical diagnosis of sporotrichosis was made and treatment with aureomycin instituted. The patient received 1 Gm. a day for two weeks; there was little, if any, clinical response to this therapy. On Jan. 3, 1950, treatment with potassium iodide was instituted.

Direct smears made from the pus and stained by Gram's method revealed no organisms. Four culture tubes were planted with specimens from the direct smear and from the expressed pus. In four days numerous colonies were noted. Three days later characteristic forms of sporulation were seen and the culture mounts were characteristic for sporotrichosis.

Sporotrichosis: Inoculation on the Palpebral Conjunctiva with Descending Nodular Lymphangitis. Presented by DR. EMANUEL MUSKATBLIT and (by invitation) DR. JOSEPH I. SINGER.

K. E., aged 11 years, had played amongst some salt meadow hay used to mulch bulbs on a tulip farm near Babylon, L. I., two to four weeks prior to the onset of the infection. The mother remembers brushing the hay off the face and out of the hair. Symptoms appeared on or about Nov. 30, 1949. The family physician made a diagnosis of conjunctivitis and administered 2,700,000 units of penicillin parenterally. There were swelling and redness of the lids and conjunctiva. There was no improvement, and the patient was referred to an ophthalmologist who noted granulations on the lower right palpebral conjunctiva and thought that the patient might have a chalazion. Two days later (December 15) the upper lid became swollen. On December 17 there was preauricular lymphadenopathy and a chain of nodes was seen on the cheek. Dr. Singer was called in on consultation, and the possibility of sporotrichosis was considered. A request was made to obtain material for culture. On December 31 the upper lid was incised and a thick green purulent material exuded. The patient is asymptomatic.

Examination revealed on the inner aspect of the right lower lid at the lateral border two adjacent white papules the size of a hemp seed. The entire upper lid is red and swollen. Along the lateral border of the lower lid there is a group of small red nodules. On the cheek over the zygoma there are four distinct deep rubbery nodules ranging in size from that of a cherry to that of a pea. They are flesh colored or slightly erythematous. No regional adenopathy is palpated.

Examination of the smear of the pus revealed no fungi or bacteria. There were many pus cells seen. The Giemsa stain for Rickettsia was negative. Bacteriologic culture grew a pure strain of hemolytic Staphylococcus albus.

On Sabouraud's glucose agar a definite colony, 1 cm. in size, was seen on the eighth day. The central portion was brown and wrinkled while the periphery was cream colored and filamentous. Culture mount revealed fine myceliums with ovoid and round conidia borne on lateral branches. Clusters of spores or rosette formations were also seen.

The patient has received aureomycin and potassium iodide. After the diagnosis was established, the dose of potassium iodide was increased to 30 drops three times daily. The nodes have become confluent and fluctuant and are decreasing in size. The palpebral lesion is disappearing.

DISCUSSION ON CASES OF SPOROTRICHOSIS

DR. FREDERICK REISS: Dr. Muskatblit's cases are interesting, and the source of infection rather unusual. Subterranean sporotrichosis has not been known in this country, and I imagine the case of J. D. is the first case of this infection to be contracted while the patient was working in a sewer. In this connection mention should be made of an epidemic outbreak of sporotrichosis in South African gold mines, as reported by DuToit (*South African M. J.* **15:** 71, 1941). Over 650 cases have been reported, and the source of infection was traced to decaying timber.

DR. ALEXANDER A. FISHER: I should like to discuss Dr. Singer's case. About three years ago I presented an exact replica of this case, and similar cases were reported by Dr. John Graham from the Long Island area. My patient got the infection from lettuce which he was handling. He did well on treatment with potassium iodide.

DR. F. P. MERKLEN, Paris, France (by invitation): No cases of sporotrichosis have been seen in France for a long time. The same can be said of the mycoses. I had to visit America to see these cases. It has been interesting to hear from Dr. Fisher that the previous cases all came from the same locale. Most of the cases described as observed in France had their origin in Switzerland; in the past many were seen in France, but no longer.

DR. EMANUEL MUSKATBLIT: I was tremendously surprised to hear from our French colleague that for the past 10 years there has not been any such case reported in France. From our textbooks I gained the impression that sporotrichosis was especially widespread in France. I should like to stress the point raised by Dr. Reiss that the subterranean source of infection is rare, except for the just mentioned South African cases. The first patient worked in a sewer and encountered decaying vegetable material. The case is considered compensable because the injury sustained while digging a sewer preceded the development of the disease. The sporotrichosis followed late after the trauma, but it did follow, and this fact is taken as a point in favor of the compensability of this case.

DR. JOSEPH I. SINGER (by invitation): The cases mentioned by Dr. Fisher (excluding his own) were reported by Dr. Graham (ARCH. DERMAT. & SYPH. **54**:726, 1949) and included those of about six or more patients from Patchogue, Long Island, about 75 miles from this city; the source was the same salt hay in all these cases. Since the case presented tonight came under my observation, I have heard of another patient in whom there developed a similar eruption from hay.

Lichen Planus et Acuminatus Atrophicans (Feldman); Lichen Planopilaris (Pringle).
Presented by DR. JULIUS H. POLLOCK.

B. B., aged 74, a cabinetmaker, noted the appearance of an eruption on the scalp about four years previously. About six or seven months ago lesions appeared on the left arms and subsequently on other parts of the body.

On the scalp, mainly on the vertex and extending outward, there are isolated and coalescent depigmented, smooth, slightly depressed, shiny atrophic areas, marked by total hair loss. These areas vary in size from about 1 to 3 cm. Some of the borders of those lesions show slight erythema and violaceous color, and nearby dilated follicles may be seen. In between these atrophic areas and at the borders, the skin has a nutmeg grater feel and shows numerous dilated follicles filled with brownish or blackish horny plugs. When these plugs are removed, depressed openings the size of a pinhead are left at the follicular sites.

On the outer aspects of the left arm, right flank, right buttock and slightly on the left thigh there are discrete minute acuminate brown or black papules. Each one of these shows a horny plug, which is removed with difficulty and on removal leaves a crater in the center of each papule. No lesions on the oral mucosa or on the glans penis have been noted.

Histological examination of a lesion taken from the scalp showed a noticeable increase of the loose laminated horn which formed plugs in considerably dilated follicles. Side walls of the follicles were thin and stretched, but their bases were somewhat acanthotic and showed a mild degree of hypergranulosis. Immediately under the epidermis there was a thin band of collagen which contained horny and scattered pigment granules and which separated the epidermis from the infiltrate throughout the section except at the base of the follicular rete peg, where the basal cell margin was washed out as a result of the banal, chiefly small round cell cellular reaction. Similar massed collections were found from the subepidermal region to the midcutis in relation to, but not completely fused with, the follicles.

The Weigert stain showed almost normal distribution of the elastic tissue except that it was pressed aside and not present in the areas of the inflammatory infiltrate.

Examination of a lesion taken from the arm showed the same picture as detailed above.

DISCUSSION

DR. MAURICE UMANSKY: Lichen planus et acuminatus atrophicans consists of a triad of symptoms: lichen planus lesions, lichen spinulosus lesions and alopecia cicatrisata of the scalp. The element of lichen planus is missing in the presented case. There is no clinical evidence of it, nor was it demonstrated histologically. For that reason, the presented case cannot be considered lichen planopilaris. This case would rather support Little's original contention of the occurrence of cases of lichen spinulosus and folliculitis decalvans, in which the presence of lichen planus is not essential.

DR. FREDERICK REISS: I agree with Dr. Umansky that there is neither histological nor clinical evidence for the diagnosis. This patient has lichen-pilaris-like lesions which are

histologically well described. The histopathological changes are not so characteristic that they may be labeled lichen planus. The question arises of how to explain the alopecia. I believe that such a process can be associated with lichen pilaris. In fact, that condition frequently ends in an atrophic process. A good many cases were reported of lichen pilaris decalvans which would fit in with the clinical picture. I do not find evidence of typical lichen planus.

DR. HENRY SILVER: I fully agreed with Dr. Pollock's designation of his case as lichen planus et acuminatus atrophicans. It seems to me that the variants of this disease are not generally recognized. Dr. Umansky and Dr. Reiss are under the impression that these cases must present elements of lichen planus. That has not been my experience. It is true that in textbook cases all the clinical features are present: namely, lichen planus lesions, acuminate lesions and involvement of the scalp with the characteristic alopecia. Most of the time, however, we deal with cases which do not present all the elements described. I have seen cases limited to the scalp, presenting only keratotic plugging and alopecia. At other times we have the elements shown so clearly in Dr. Pollock's case, lesions which Sir Graham Littke has mistakenly regarded as lichen spinulosus. These are not spinous lesions: they are just plugged follicles. Feldman's terminology is descriptive and should be retained and, perhaps, include the adjective "decalvans."

DR. JULIUS H. POLLOCK: Having been associated with Dr. Feldman during the years when he was particularly interested in this disease, I know that Dr. Silver's remarks justly express Dr. Feldman's understanding of this condition. If nothing else, Dr. Feldman, besides applying a title much more descriptive of the disease than any used hitherto, cleared the misconception that Dr. Little had occasioned in calling this condition folliculitis decalvans.

The biopsy specimens, both that from the scalp and that from the chest, revealed features of lichen planus so well described in Dr. Feldman and Dr. Sachs' paper. Clinically, the absence of lichen planus lesions does not invalidate the diagnosis, since these lesions may be absent, may have been present at some prior time or may later on make their appearance.

A Case for Diagnosis: Granuloma Inguinale? Presented by DR. MARTIN V. BOARDMAN.
A Case for Diagnosis: Ichthyosis Hystrix? Presented by DR. DAVID B. BALLIN.
A Case for Diagnosis: Seborrheic Dermatitis? Chronic Exudative Lichenoid and Discoid Dermatitis (Sulzberger and Garbe)? Presented by DR. MARTIN V. BOARDMAN.
Chronic Exudative Lichenoid and Discoid Dermatitis (Sulzberger and Garbe). Presented by DR. FRANCES PASCHER and (by invitation) DR. MILTON E. HELMAN.
Multiple Symmetric Nevi of the Face. Presented by DR. HANS H. BIBERSTEIN.
Xanthoma Tuberosum. Presented by DR. ABRAHAM J. ORFUSS.

Charles R. Rein, M.D., *Vice President, in the Chair*

Henry Silver, M.D., *Secretary*

Feb. 16, 1950

Lichen Obtusus. Presented by DR. ARTHUR B. HYMAN.

A. W., a white man aged 22, presents a cutaneous eruption of 11 years' duration.

Above the medial aspect of the right ankle there are irregularly shaped patches consisting of closely set globular, grayish, hyperkeratotic nodular lesions. Routine laboratory examination showed no abnormalities.

The histological examination showed a thick horny layer following the indentations of a rugose skin. The epidermis was definitely thickened with some elongation of the rete pegs. The vessels of the upper third of the cutis showed considerable swelling of their walls and were sharply surrounded by an infiltrate, mainly histiocytic.

No amyloidosis was found in slides stained for amyloid.

DISCUSSION

DR. WILBERT SACHS: The patient has a papular neurodermatitis which is hyperkeratotic. The term lichen obtusus is antiquated.

DR. LOUIS CHARGIN: It strikes me that this disorder is either lichen planus or a papular form of neurodermatitis. At this late stage it is impossible to make a diagnosis on purely clinical or even histological grounds. It would be well worth following these patients early in the disease

to see whether any of these cases have primarily elements of lichen planus, for it is known that in hyperkeratotic lichen planus the characteristic picture is lost.

DR. PAUL GROSS: Dr. Hyman's presentation brings up an important question. I have often wondered whether the cases which we used to diagnose as lichen moniliformis in former years would be recognized today as lichen amyloidosus. As shown in Dr. Hyman's case, they would not necessarily be. Although it is difficult to differentiate this type of eruption from lichen planus, I am inclined to agree with those who consider it a variant of lichen simplex chronicus.

DR. MAX JESSNER: In the German literature lichen obtusus is usually regarded as a form of lichen planus. In the French literature the disorder is known as lichen obtusus verrucosus and under many other names. The French do not regard it as lichen planus because its histological picture is so different from that of lichen planus. It is included in the neurodermatitis group. This question has been discussed for many years and is still debatable. The case presented could be thought of clinically as lichen amyloidosus, but there is no amyloid to be found. There may perhaps be some chemical method to disclose the amyloid, if present, and I wish that Dr. Herrmann would enlighten us.

DR. FRANZ HERRMANN: It is hardly necessary to suggest that several, and not only one, of the staining methods for amyloid should be employed to exclude its presence with certainty.

DR. CHARLES A. GREENHOUSE: Some 15 years ago I presented a case before this Society with the diagnosis of lichen ocreaformis (ARCH. DERMAT. & SYPH. **32**:513, 1935). In my case the lesions were almost identical with those in Dr. Hyman's case except that they were more extensive and assumed the configuration of a skin guard. The case was studied by the late Dr. D. L. Satenstein, who was able to demonstrate the presence of amyloid.

DR. ARTHUR B. HYMAN: Apart from the diagnosis of amyloidosis usually made in these cases, I find various names, often lichen planus ocreaformis, recorded in the literature for a number of similar cases. Histologically, there is no evidence of lichen planus. Ocreaformis is a good descriptive term, meaning "legging," introduced by Lieberthal. Those of the French school place the disease in the neurodermatitis-prurigo group. All that can be offered is the descriptive term because the condition is not amyloidosis, there is little evidence of its being neurodermatitis and sections show no evidence of lichen planus. I wanted to avoid the term lichen moniliformis because some cases have been confused with the condition described by Rein and Wise.

A Case for Diagnosis: Dermatitis Herpetiformis? Erythema Annulare Centrifugum?
Presented by DR. CHARLES R. REIN and (by invitation) DR. B. L. SNIDER.

J. C., a woman aged 25, presents a widespread eruption which began two years ago. She first noticed lesions on the arms about 10 days before each menstrual period. These lesions would clear almost completely within a week after the menses stopped. Her menses began at the age of 12 years, were regular until the age of 20 and then became irregular. The present eruption began with pregnancy five months ago and has persisted and become widespread.

The eruption involves the abdomen, arms and thighs. The lesions begin as inflammatory papules the size of a pea, which coalesce and spread peripherally. On the abdomen there is a large annular lesion 3½ inches (9 cm.) long with a raised, actively erythematous border and a clear, pigmented center.

During the two months of observation, all incidental drugs were eliminated and numerous medications tried. The patient was placed on an "iodide free" diet. There was some improvement, but new outbreaks have occurred accompanied with severe pruritus. Results of a microscopic examination for fungi were negative.

Patch tests with 20 per cent potassium iodide and potassium bromide with controls were done on an uninvolved area of the back and a previously affected area of the abdomen. A reading in 48 hours revealed a definite positive reaction to potassium iodide and potassium bromide on the previously affected area on the abdomen, while the reaction on the back was negative.

Fractional doses of superficial roentgen ray therapy (75r) resulted in improvement of the treated area following two exposures. There has been no response to the administration of bismuth parenterally, repeated autohemotherapy and the use of antihistaminic medication (chlorprophenpyridamine [chlor-trimeton®] maleate) and sodium thiosulfate. Sulfapyridine was not tolerated, even in small doses. In recent weeks potassium arsenite (Fowler's) solution, diluted 1:3, was tried but was not well tolerated.

The abdominal eruption has subsided, but new lesions have developed on the neck, periorbital areas and hips, and nummular vesicular areas have appeared recently on the left arm.

DISCUSSION

DR. HENRY SILVER: Do vesicular lesions occur in erythema annulare Darier?

DR. LOUIS CHARGIN: The case impresses me as one of Darier's annular erythema. Some of these cases have proved to be mycosis fungoides. I have presented on several occasions such a case before this Society (for example, ARCH. DERMAT. & SYPH. **40**:1025, 1939).

DR. MAX JESSNER: In answer to Dr. Silver, vesicular lesions rarely occur in typical erythema annulare of the Darier type. I had occasion to see this patient and thought of Darier's type of erythema annulare. I recalled that Gougerot was in favor of putting this form of erythema into the dermatitis herpetiformis group. I had discussed this problem with him. Since the patient has had this eruption during pregnancy as well as during the menstrual periods, I am inclined to regard it as dermatitis herpetiformis. The patch test reactions were positive only in the healed but still pigmented lesion. This observation shows that in suspected cases of dermatitis herpetiformis one has to apply the potassium iodide and potassium bromide patch tests not only on normal skin but also on affected and healed skin. At present the patient has rings of blisters in the involved areas, so that the diagnosis of dermatitis herpetiformis is justified.

DR. FREDERICK REISS: May I draw your attention to the vesicular type of Darier's erythema which is mentioned in the article of Dr. T. Graham on erythema annulare centrifugum (ARCH. DERMAT. & SYPH. **22**:786, 1930). I agree with that diagnosis, and I believe this is an authentic case.

DR. WILBERT SACHS: A biopsy should be done to rule out dermatitis herpetiformis. I am quite certain it will.

DR. CHARLES WOLF: I suggest the diagnosis of erythema multiforme for the following reasons: the spontaneous involution of the lesions, the repeated attacks without scar formation and the fact that the condition has appeared on and off for two years without residual pigmentation. Furthermore, in erythema annulare Darier I have never seen any bullous or vesicular lesions. Whether Dr. Graham's cases (referred to by Dr. Reiss) were proved I do not know, but I believe that the classic description of Darier's erythema does not include bullous lesions.

DR. PAUL GROSS: I agree that this eruption clinically conforms to the diagnosis of herpes gestationis. It is not warranted to consider all bullous eruptions occurring in pregnancy as Duhring's disease. The eruption in this case could just as well be erythema bullosum, but the differential diagnosis should depend on the therapeutic test with sulfapyridine.

DR. HENRY SILVER: The clinical impression of this eruption is one of erythema annulare Darier. The vesicular lesions puzzled me. Perhaps the pregnancy is responsible for the appearance of these lesions.

DR. JULIUS H. POLLOCK: The history and the time relationship of those eruptions to the menstrual cycle and the persistence of the condition during pregnancy point to a hormonal etiology. That the eruption disappears with a concomitant drop in blood estrogen and that it persists during pregnancy, when the estrogen levels are elevated, are factors to be considered in the condition. While the patient is pregnant it might be safe to try large doses of corpus luteum, and after pregnancy it might be of value to use either corpus luteum or testosterone as an antagonizer, premenstrually.

DR. CHARLES R. REIN: The patient has been under the care of an endocrinologist and gynecologist. She states that the lesions which occurred 10 days prior to each menses during the past two years were similar to those she has had during this pregnancy. It is also of interest to note that a few days ago there was an exacerbation of the eruption within a few hours after the ingestion of sea food; this observation is also suggestive that the present eruption belongs to the group of dermatitis herpetiformis.

DR. B. L. SNIDER (by invitation): We designated this case as dermatitis herpetiformis rather than herpes gestationis because the same or a similar eruption had occurred intermittently prior to each menstruation for two years. The eruption has been erythematous and edematous, with vesicles having been noted only in recent weeks. Itching has been severe and worse with each exacerbation.

Lichen Nitidus and Lichen Planus with Unusual Histological Features. Presented by Dr. David Bloom.

L. B., a man aged 19, registered at the Skin and Cancer Unit of the New York University–Bellevue Medical Center on Jan. 6, 1950, complaining of an eruption of about two months' duration. Subjective symptoms are absent.

Over each elbow there is a scaly plaque the size of a 25 cent piece, extending downward toward the ulnar region of the forearm. Around these plaques there are reddish or skin-colored papules the size of a pinhead or pinpoint. On the wrists there are grouped slightly reddish papules, in addition to lentil-sized round and angular violaceous papules with distinct umbilication. On the shaft of the penis there are violaceous angular and round lesions the size of a pinhead.

Histological examination of a section taken from the left elbow showed a definite structure of lichen nitidus. A section taken from a lesion on the wrist was reported by Dr. C. H. Miller as "lichen-planus-like lesion containing epithelioid cells in the inflammatory infiltrate." The following description was given: The epidermis was acanthotic, and the granular layer and the horny layer were increased in thickness. The upper third of the cutis had an inflammatory infiltration consisting of round cells, wandering connective tissue cells and many epithelioid cells. The last-mentioned were located mostly in the subepidermal zone.

DISCUSSION

Dr. Wilbert Sachs: I have examined one slide, which shows typical lichen nitidus. However, clinically the lesions suggest lichen planus. Because of this situation, further histological studies should be made. There are no epithelioid cells in lichen planus.

Dr. Max Jessner: About two years ago we had similar discussions on this subject, namely whether or not lichen planus and lichen nitidus are one and the same disease. In my experience, epithelioid cells and giant cells are occasionally found in lichen planus.

Dr. Arthur B. Hyman: The lesions which are clinically lichen planus but histologically lichen nitidus should be regarded as lichen nitidus with atypical clinical appearance rather than lichen planus with atypical histological features.

Dr. David Bloom: This patient presents clinically the association of lichen nitidus and lichen planus. Histologically the presence of many epithelioid cells in the infiltration of the lichen planus lesion represents a transition between lichen planus and lichen nitidus. This case, in addition to other cases in the literature, forces one to consider lichen planus and lichen nitidus closely related.

Tinea Capitis Due to Trichophyton Violaceum. Presented by Dr. Emanuel Muskatblit.

A white boy aged 5 years is a patient at the Skin and Cancer Unit of the New York University-Bellevue Medical Center. The first signs of the disease were noticed in September 1949. The eruption was diagnosed elsewhere as seborrheic dermatitis and was treated without benefit.

On the scalp there are several small, poorly defined foci with faint redness, scaling and a small number of hairs in the form of black dots resembling comedos. Similar hairs were also found on apparently normal skin of the scalp.

Microscopic examination of the black dots in a sodium hydroxide preparation showed fragments of hairs filled with large spores (endothrix). Cultures produced Trichophyton violaceum.

Inflammatory Ringworm of the Scalp Caused by Trichophyton Sulfureum. Presented by Dr. Andrew G. Franks and (by invitation) Dr. Ernst Rosenbaum.

J. O., a boy aged 7 years, was first seen by us on Jan. 19, 1950. The mother states that a week after a haircut there developed an irritation of the scalp. The lesions have been present for the past two weeks. The patient was treated with penicillin tablets by his own physician.

On the occipital part of the scalp there are numerous deep abscesses ranging in size from that of a pea nearly to that of a chestnut (kerion celsi). On the right leg there is an extensive

eruption of grouped pustules and bluish small deeper nodules (trichophytid and erythema nodosum).

The trichophytin test in a dilution of 1:30 elicited a positive reaction after 48 hours. Repeated examinations under the Wood light revealed no fluorescence. Microscopic examination of the hair showed no organisms. The culture medium inoculated with scales from the scalp grew Trichophyton sulfureum.

DISCUSSION ON CASES OF RINGWORM OF THE SCALP

DR. EMANUEL MUSKATBLIT: The cases of tinea capitis due to Trichophyton violaceum differ from the common form caused by Microsporum audouini. In T. violaceum tinea one does not find large, well demarcated patches with abundant scaling and many broken-off hairs. In spite of five months' duration, the lesions in the case presented now are small and discrete; there is little or no scaling, and the diagnosis is difficult because it is not easy to see the infected hairs which are present in the form of black dots and which do not fluoresce under Wood's light. One has to find and pick off these black dots to make the diagnosis. These cases are difficult to eradicate. They are resistent to chemical medication and require roentgen ray epilation and thorough after-care. When all hairs fall out one sees many black dots of infected hairs on the scalp. They will not fall out spontaneously and have to be picked off by mechanical means, such as peeling or scrubbing, in order for a recurrence to be prevented.

Generally speaking, one should not associate the trichophytin reaction with the species of fungus. Actually the name of the species does not predetermine what kind of reaction one will get. For instance, in torpid cases due to M. audouini there is usually a negative or a weakly positive reaction. In kerion, however, caused by the same fungus, a strongly positive reaction is obtained. The same variety of reactions occur with Trichophyton sulfureum. The trichophytin reaction occurs parallel with the spontaneous reaction of the skin in the lesions but not parallel with the particular species causing the condition.

Keratoderma Climactericum (Haxthausen's Disease). Presented by DR. JOHN GARB.
Granuloma Inguinale Resembling Carcinoma. Presented by DR. JULIUS H. POLLOCK.
Recurrent Basal Cell Epithelioma. Presented by DR. JULIUS H. POLLOCK.
Plastic Induration of the Penis. Presented by DR. ERNEST W. NATHAN.
Pityriasis Rubra Pilaris. Presented by DR. CHARLES R. REIN and (by invitation) DR. B. L. SNIDER.
Generalized Acne Varioliformis. Presented by DR. ABRAHAM J. ORFUSS.
A Case for Diagnosis: Necrobiosis Lipoidica? Granuloma Annulare? Presented by DR. MARTIN V. BOARDMAN.
Atrophoderma-Vermicularis-Like Picture Following Lupus Erythematosus. Presented by DR. FREDERICK REISS.
Unusual Pigmentation. Presented by DR. ABRAHAM J. ORFUSS.
Atrophy and Leukoderma Following Lichen-Planus-Like Eruption Due to Gold Therapy. Presented by DR. ELLEN REINER.
A Case for Diagnosis: Lymphoblastoma? Presented by DR. MARTIN V. BOARDMAN.
Lichenoid Sarcoid. Presented by DR. JOSEPH L. MORSE.
Pemphigus Erythematosus (Senear-Usher). Presented by DR. DAVID BLOOM.

PHILADELPHIA DERMATOLOGICAL SOCIETY

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Jan. 21, 1950

Squamous Cell Epithelioma of the Lower Lip. Presented by DR. BERTRAM SHAFFER and (by invitation) DR. THEODORE EBERHARD and DR. WILLIAM WELLS.

Biopsy on April 11, 1949 was reported as showing squamous cell epithelioma. Treatment consisted in the daily administration of roentgen radiation, from April 20 to May 4, 1949, with the following technical factors: 120 kv. (peak), 10 ma., 3 mm. Al filtration and 20 cm. skin-target distance. Fractionated doses—four of 200 r, four of 300 r and five of 400 r—were given for a total dose of 4,000 r. Clinical cure resulted.

Basal Cell Epithelioma. Presented by DR. BERTRAM SHAFFER and (by invitation) DR. THEODORE EBERHARD and DR. WILLIAM WELLS.

Biopsy on Oct. 18, 1949, was reported as showing basal cell epithelioma. Treatment consisted in the daily administration of roentgen radiation, from Oct. 26 to Nov. 9, 1949,

to both areas, with the following technical factors: 120 kv. (peak), 10 ma., 3 mm. Al filtration and 20 cm. skin-target distance. Fractionated doses—four of 200 r, four of 300 r and five of 400 r—were given, for a total dose of 4,000 r to each lesion. Clinical cure resulted.

Basal Cell Epithelioma, Left Cheek. Presented by DR. BERTRAM SHAFFER and (by invitation) DR. THEODORE EBERHARD and DR. WILLIAM WELLS.

Biopsy on May 11, 1949 was reported as showing basal cell epithelioma. Treatment consisted in the administration of roentgen radiation daily, from May 18 to June 2, 1949, with the following technical factors: 120 kv. (peak), 10 ma., 3 mm. Al filtration and 20 cm. skin-target distance. Fractionated doses—four of 200 r, four of 300 r and five of 400 r—were given, for a total dose of 4,000 r. Clinical cure resulted.

Squamous Cell Epithelioma, Right Pinna. Presented by DR. BERTRAM SHAFFER and (by invitation) DR. THEODORE EBERHARD and DR. WILLIAM WELLS.

Biopsy on Sept. 27, 1949, was reported as showing squamous cell epithelioma. Treatment consisted in the daily administration of roentgen radiation, from Oct. 4 to Oct. 18, 1949, with the following technical factors: 120 kv. (peak), 10 ma., 3 mm. Al filtration and 20 cm. skin-target distance. Fractionated doses—four of 200 r, four of 300 r and four of 400 r—were given, for a total dose of 3,600 r. Clinical cure resulted.

Basal Cell Epithliomas, Nose. Presented by DR. BERTRAM SHAFFER and (by invitation) DR. THEODORE EBERHARD and DR. WILLIAM WELLS.

Biopsy on Oct. 4, 1949 was reported as showing basal cell epithelioma on each side of the nose.

Basal Cell Epithelioma, Left Cheek Below the Eye. Presented by DR. BERTRAM SHAFFER and (by invitation) DR. THEODORE EBERHARD and DR. WILLIAM WELLS.

Biopsy on Aug. 15, 1949 was reported as showing basal cell epithelioma. Treatment consisted in the administration of roentgen radiation daily, from Aug. 24 to Sept. 8, 1949, with the following technical factors: 120 kv. (peak), 10 ma., 3 mm. Al filtration and 20 cm. skin-target distance. Fractionated doses—four of 200 r, four of 300 r, one of 400 r and four of 500 r were given, for a total dose of 4,400 r. Clinical cure resulted.

Cavernous Hemangioma, Left Labium Majus, Treated with Radium. Presented by DR. BERTRAM SHAFFER and (by invitation) DR. THEODORE EBERHARD and DR. WILLIAM WELLS.

DISCUSSION OF CASES OF EPITHELIOMA AND HEMANGIOMA

DR. MORRIS IVKER (by invitation): Dr. Eberhard has over a period of years developed the technic presented as a result of trial and error. He advocates a fractionating method of treatment starting with a small dose of 200 r and ending with a dose of 400 r in air. The treatment is begun with 200 r daily for four days, and then four treatments of 300 r and then five treatments of 400 r are given, for a total of 4,000 r in air. If the lesion is large, i. e., more than 2.5 cm., the total dose is reduced to 3,600 r, in view of the greater back scatter to the skin in the larger area. The total skin dose remains approximately the same. Two of the patients were shown because of the prevalent conception that treatment of lesions around the ear always produces chondritis. That concept is now falling into disrepute. Recently in the radiologic literature there was an article on treatment with roentgen rays' producing better results than surgical measures, an attempt being made to preserve as much of the normal tissue as possible.

The man with the lip lesion was shown to demonstrate the shield which was hung on the lip, protecting the tissues behind the lip and exposing the lesion, with sufficient margin. It is very simple to make—merely a straight piece of lead cut out into a hemisphere. My associates and I use it to protect the teeth, the alveolar ridge and the gingival surface.

DR. J. P. GUEQUIERRE: I congratulate the men who did this work. The results are excellent. Patients treated with radium and roentgen rays should be observed at frequent

intervals, for at least five years, because certainly one is more likely to get sequelae from irradiation than from other methods of treatment. It is a question whether or not there will be changes in the patients with lesions on the lip, the nose and the ear. I think all of us have seen excellent results also from electrocautery, use of the current and use of trichloroacetic acid. I do not think that there is any one best method of treating cutaneous cancer. I think the method one is most familiar with is the method to use. The use of electrosurgery or scalpel surgery, if the lesion is not too large, is excellent, and with it treatment is all done at one sitting. What is the rationale of the dosage employed? In the lip case, I asked the man whether there was any reaction after this treatment and he said there was not. That observation is unusual, for there is usually a sore mouth. The shield is a very good idea.

DR. MORRIS IVKER (by invitaton): Edema of the lip, but very seldom irradiation reaction on the alveolar process, is produced by the use of this method. With the use of 85 kv. with no filter, the percentage of depth dose drops considerably and if there is an epithelioma of any great thickness one will not get enough of a depth dose to obtain a cure. The man with the lesion on the cheek had been treated many times by other methods. Most of the scarring seen was not from irradiation. The scarring was there before treatment with radiation was started. Actually, the nodules were growing around the edge of the scar. There are failures, but my associates and I think they are far fewer with this than with any other method of therapy.

DR. THOMAS BUTTERWORTH, Reading, Pa.: I remember that 20 years ago Dr. Schamberg took a sharp curet, curetted a basal cell cancer, went over it with trichloroacetic acid to stop the bleeding and obtained a beautiful result. I do not think we should convey the idea that treatment with roentgen rays is the only treatment for cancer of the skin. I have cured dozens of cases using 85 kv., unfiltered; yet there are lesions where electrosurgery is the method of choice. I have in mind the case of an old woman with carcinoma of the scalp. The cancer has been cured by roentgen rays, but there is an ulcer in the parietal region that nothing will ever cure; the tissues are too sclerotic. If the lesion had been excised, the patient would not have had an ulcer for seven or eight years. There are some areas, such as over the eyelids, where I prefer roentgen ray therapy.

Cancer of the Nose, Postoperatively, with Prosthesis. Presented by DR. REUBEN FRIEDMAN and (by invitation) DR. JOSEPH SQUILLACE.

M. H., a white woman aged 61 years, was previously presented for therapeutic suggestions concerning the extensive carcinoma of her nose. In May 1949 the growth was destroyed by surgical diathermy (electrocoagulation). The patient now wears a plastic appliance (soma prosthesis) over her nose.

Pseudopelade of Brocq. Presented by DR. CARROLL S. WRIGHT and (by invitation) DR. K. SMITH.
Alopecia Areata of Possible Psychogenic Origin. Presented by DR. JOHN P. SCULLY, Reading, Pa.
Cutaneous Amyloidosis, Localized to the Cheek. Presented by DR. JOHN M. SIEGEL.
Rhinophyma, Postoperatively. Presented by DR. REUBEN FRIEDMAN and (by invitation) DR. JOSEPH SQUILLACE.

Captain Robert L. Gilman (MC), U.S.N., *Chairman*

H. E. Twining, M.D., *Secretary*

Feb. 17, 1950

Tuberculous Ulceration of the Hard Palate: Excision and Palatoplasty. Presented by DR. IRVING MEYER (by invitation) and DR. C. C. THOMAS.

A. A., a Negro aged 24 years, on Sept. 21, 1949, punctured his palate with a fish bone. Three or four days later a perforation developed. At the hospital a diamond-shaped perforation about 1.5 cm. in diameter was seen in the midline of the posterior third of the hard palate, extending into the nose, so that the nasal structures, i. e., the base of the vomer, were visible.

In 1944 the patient acquired pulmonary tuberculosis, for which he was treated in a sanatorium for one year and then discharged as having an arrested case. He contracted gonorrhea and primary syphilis the same year, received penicillin therapy and was told he was cured. Since then he has been in good health. His medical examination revealed no abnormality except dulness of the right lower part of the chest to percussion.

The report on the biopsy, Oct. 19, 1949, read as follows: "many nodules of epithelioid cells and giant cells showing central caseation." Smears from the ulcer on Sept. 23 and Sept. 28, 1949, were positive for acid-fast organisms.

On Oct. 21, 1949, excision of the margins of the ulcer was performed, and a palatoplasty was done at the same time. The excised marginal tissue revealed the same histological picture as had the previous biopsy specimen. The patient was treated with procaine penicillin, 300,000 units daily, from Oct. 4 to Nov. 1, 1949. He was treated with streptomycin from Sept. 28 (several weeks prior to surgical operation) to Oct. 31, 1949, and received a total of 42 Gm. Healing progressed uneventfully.

DISCUSSION

DR. FRED D. WEIDMAN: Is the diagnosis proved for tuberculosis? Why was syphilis excluded? In the photograph the perforation has such exquisitely sharp edges that it is hard to reconcile the picture with the reaction seen in tuberculosis. Usually there is a papilliferous ulcerated process around the edge. Some patients have two diseases—I wonder whether this patient has a syphilitic perforation with tuberculosis.

DR. M. H. SAMITZ: Was the lesion painful?

DR. IRVING MEYER (by invitation): The patient did not complain of pain. His reason for seeking therapy was that he spoke with a distinctly nasal tone. He removed the fish bone very simply by just reaching in and withdrawing it. The perforation took place within two weeks of the accident. It naturally occurred to us that we would have to rule out syphilis or tuberculosis. The serologic tests for syphilis and the cerebrospinal fluid examination both gave negative results. The roentgenogram showed the left lung clear. The right lung showed residual thickened pleura but no evidence of active tuberculosis. The patient had been treated for tuberculosis in 1944. The remaining observations were noncontributory. I have gone through the literature from 1850 looking for another case of tuberculosis of the palate with perforation and have as yet not found one. A tuberculous osteomyelitis of the maxilla of the alveolar border, following extraction of teeth, has been reported. I saw two other cases at the Metropolitan Hospital in New York, one a tuberculous antrum and the other a tuberculous process of the alveolar process of the maxilla, but as yet I have not seen any other perforation of the palate.

Angiokeratoma. Presented by DR. MEYER L. NIEDELMAN and DR. ADOLPH H. BLEIER.

M. N., a Negro aged 28 years, presents on the anterior and medial aspect of the right thigh a large, indurated lesion 10 to 15 inches (25 to 37 cm.) in diameter, the surface of which is hyperkeratotic and, to a great extent, verrucous. It bleeds easily on slight trauma. At the periphery there are numerous bluish red nodules of various sizes, partly soft and partly with a hyperkeratotic surface. No telangiectasias are visible in the surrounding skin. Intermixed with the verrucous lesion is keloid tissue, the result of previous surgical treatments.

The patient first acquired "warty" nodules on his right thigh at the age of 2 years. The growth became gradually larger until it reached its present size. On two occasions some of the lesion was removed (in 1931 and 1941). The patient always noticed bleeding on slight trauma, and there has been considerable drainage for the past three years.

A roentgenogram of the chest revealed no abnormality. Results of urinalysis were within normal limits, as was the blood count. Purified protein derivative, intermediate strength, gave a moderately positive reaction.

The report on the biopsy (Dr. Fred D. Weidman) read as follows: "The specimen was divided into at least three portions, this fact accounting for the varying sizes and shapes of the sections exhibited in this slide. Under the best conditions the structure of angiokeratoma was illustrated in typical form.

"Thus, the surface of the skin was so irregular as to be almost verrucous. It was covered by an excessively thick layer of extremely dense hyperkeratotic material. The rest of the epidermis was very irregularly acanthotic. Some of the pegs were, indeed, bizarre. The epithelial cells were swollen by a mild grade of intercellular edema. Of course, the heavy load of pigment in the basal cells was to be expected in a Negro. Significantly, the pigment was absent from the center of the lesion, where the disease processes were at their height.

"The papillae in the center of the lesion were hugely broadened out by dilated blood vessels, resulting in atrophy of the overlying epidermis. Red blood cells had escaped from most of them, but there were ample ones in others to establish the identity of the spaces. This identification was much needed because the spaces were lined by a single layer of endothelium and could be confused with lymphatic spaces. Thus, the processes were not hyperplastic, as in the case of genuine neoplasms, but the vessels were simply ectatic. Immediately underlying the ectatic vessels there were others which had an elongated form; they could be traced downward as far as the midcorium. In all cases the linings were of the simple, nonhyperplastic type already indicated.

"There was not any inflammatory infiltration or edema of significance. The capillaries in the subepidermal region were slightly hyperplastic on either side of the lesion."

DISCUSSION

DR. FRED D. WEIDMAN: This is a remarkable case. Clinically, I do not see how anyone could diagnose it as angiokeratoma, but of course the patient has had two operations. We do not know how extensive those operations were, and the patient is evidently a keloidal subject. In fact, there is one very large fibrous cord extending apparently along the line of the saphenous vein into the groin. It is almost like wood. One could almost lift this mass of indurated tissue with the hand and shove it around. It is infiltrating under the sound skin far and wide. It is a great mass of hard, woody tissue about the size of a small football. The section I examined was taken from the superficial part, consisting only of skin, and histologically it was classic for angiokeratoma. The slide was projected on the screen at the Valley Forge General Hospital, and the residents promptly diagnosed the condition from the screen. The keloidal changes explain the discrepancy between the histological report and the clinical report. Really, the answer can be made only after a biopsy specimen 2 or 3 cm. down in the depths of the lesion has been taken. I would recommend a second biopsy made by a surgeon, away down deep.

DR. MEYER L. NIEDELMAN: When Dr. Bleier asked me to see this patient with him, my first impression was that the disorder was tuberculosis verrucosa cutis. I was so sure that I put the patient on treatment with calciferol. However, in looking back and going over the history, I think that the diagnosis can be reconciled with angiokeratoma. The patient has had this condition since the age of 2 years. Of course, this lesion was electrocoagulated in 1931 and again in 1941, and so the picture today is distorted and perhaps the induration and fibrosis are due to the electrocoagulation. We took a lesion from an area that had not been electrocoagulated, and the histologic picture is probably a true one. Angiokeratomas have been described as being decidedly verrucous, though I would never make the diagnosis clinically on the basis of the appearance of the lesion tonight.

Bullous Pemphigus (Treated with Roentgen Rays to Viscera); Ocular Pemphigus, Left Eye. Presented by DR. CARMEN C. THOMAS and (by invitation) DR. H. E. PIERCE.

NOTE.—This patient died of pneumonitis in April 1950.

DISCUSSION

DR. CARMEN C. THOMAS: This patient was one of a series treated by Dr. Greenbaum with an experimental form of treatment which included 250 r of radiation filtered through copper, 0.5 mm., and aluminum, 1 mm., to the spleen, liver and heart, with supposedly enough time to allow one complete circulation of blood through the heart. This treatment is purely experimental and based on a report by Drs. Macht and Ostro. In the patients on whom it was tried—about four—there was at least some temporary relief, but all of them relapsed, and one has died.

DR. R. REFOWICH (by invitation): One of the patients now being treated in the Graduate Hospital still has an occasional bulla, but he is in comparatively good condition, and it is almost three years since he was treated. The patient presented today was in fairly good condition until two weeks ago, when she had a flare-up. Until that time there had been only

occasional bullae in the inguinal region. Out of four or five patients, these two are the only ones still living. One died of acute nephritis and another of pneumonia. I do not know what happened to the others.

DR. HERMAN KLINE, Atlantic City, N. J.: At the time of Dr. Macht's report on his 12 cases of pemphigus treated by visceral irradiation, we had two of the 12 patients in Atlantic City. One died, and one is still living. We sent the serum of the one who died to Dr. Macht in Baltimore, and it showed detoxification after treatment. The method employed was irradiation over the liver and spleen only, a very small dose, 90 r through 0.5 mm. of copper and 1 mm. of aluminum, with only one or two treatments. Dr. Macht examined the serum before and after the irradiation and reported the index lowered. In both cases the serum had been detoxified.

Neurofibromatosis (Von Recklinghausen). Presented by DR. MEYER L. NIEDELMAN.

G. G., a white boy aged 5 years who has not had any of the usual childhood diseases, is well nourished and mentally alert. He presents over the left scapular and shoulder areas an elevated, yellowish brown pigmented mass which on pressure and palpation reveals soft and hard individual masses from the size of a millet seed to that of a marble. There is no pain on pressure. The pigmentation overlying this mass is both discrete and confluent. Scattered over the body are numerous circinate and oval brownish pigmentations (café au lait) spots. These vary from 0.5 cm. to several centimeters in diameter. There are several small neurinomas scattered over the lower extremities and the neck. At his birth the mother noted several brownish and yellowish areas on his body and over the left scapular area, which she described as freckles. The mother and father are well and mentally alert. A brother, aged 9 years, has cerebral palsy.

DISCUSSION

DR. H. H. PERLMAN: I agree that this is von Recklinghausen's disease. On palpation the masses of subcutaneous nodules give the impression of lipoma. The whole picture, apart from the pigmentation, is quite a contrast to what we ordinarily see in the adult with von Recklinghausen's disease.

DR. THOMAS BUTTERWORTH, Reading, Pa.: I think this picture may be explained on the basis of von Recklinghausen's disease. First, there are fibromas and then pigmentary changes. Of the pigmentary changes occurring with von Recklinghausen's disease, the well defined café au lait spots, often containing litle brown points scattered over them, are the best known. But often, too, in von Recklinghausen's disease there are areas of freckling where freckling does not usually occur. In one case that I recall freckling was present over the flank and over the hip. A third type of pigmentation is such as is exhibited tonight—a large brown patch shading off into the surrounding skin. I have never seen these spots in this particular area before. I have seen them on the inside of the thigh and on the inner aspect of the arms but not on the top of the shoulders. The mass over the left shoulder feels for all the world like a plexiform neuroma. I have read that if one cuts into these they are likely to recur in sarcomatous form. Many physicians do not believe that a diagnosis of von Recklinghausen's disease should be made by biopsy if there is enough clinical evidence to make the diagnosis. I think that we have enough evidence to make a diagnosis of von Recklinghausen's disease here and also to explain every lesion the boy has, and I see no need for biopsy; but, if someone is curious, then he should cut into the cutaneous lesions and stay away from the plexiform neurofibromas.

DR. HARVEY BLANK: I saw a patient with lesions similar to this, but distributed over the thorax and sacral region, who also had café au lait spots. He subsequently manifested adenoma sebaceum of the face and the typical features of adenoma sebaceum. Has Dr. Butterworth seen that happen?

DR. THOMAS BUTTERWORTH, Reading, Pa.: I do not believe that there is any relationship between von Recklinghausen's disease and adenoma sebaceum. There are collagenous plaques on the trunk in most cases of adenoma sebaceum. So often these cases are presented with a 15 line histological report differentiating them from multiple benign cystic epithelioma when all that one needs to do is take the patients' shirts off and look at the plaques on their

backs and the answer is clear. The plaques on the back in adenoma sebaceum are not neurofibromas. They are made up of collagenous bundles and do not resemble von Recklinghausen's disease at all. There is no doubt that the two diseases are different, even with regard to the personality of the patients.

DR. FRED D. WEIDMAN: I should like to call attention to the hairy lesion just below the left shoulder. There is a good deal of substance under that. One can pick up a tumor apparently extending down a centimeter or two into the subcutaneous fat; in the depths it feels like lobules of fat. Did Dr. Butterworth think that the plexiform neuroma? It certainly was not tender. In von Recklinghausen's disease there are lipomas in addition to the fibrous tumor. One has been described in the wall of the urinary bladder and in other involuntary muscle tissue, and there is no reason why a lipomatous collection should not accumulate in the skin, as well, in von Recklinghausen's disease. Personally, I would not hesitate to perform a biopsy on this hairy lesion on the back. I do not think doing so would mean anything contrary to the welfare of the patient.

DR. J. M. SCHILDKRAUT, Trenton, N. J.: About 25 years ago I presented a boy here as having an abortive type of von Recklinghausen's disease. All he had were the *café au lait* spots. I followed him over the years, and he finally manifested typical von Recklinghausen's disease with numerous tumors. He has had several excised without untoward results. He has gone to other places, where he has had them electrodesiccated. Some are partially gone, and some have been entirely destroyed, and apparently he has not manifested any sarcomatous changes.

DR. THOMAS BUTTERWORTH, Reading, Pa.: I think the greatest danger in von Recklinghausen's disease is cutting into the plexiform neuromas, not so much the individual lesions. I have excised the latter occasionally myself. Regarding the café au lait spots developing into neurofibromas, in 1934 we had 50 patients with coffee spots without tumors of any kind at the Pennhurst School for feebleminded persons. Fifteen years later, 34 of them were reexamined and still had coffee spots without other evidence of neurofibromatosis. One patient had been pregnant, and perhaps 35 or 40 per cent of them had gone through puberty during the 15 years. Apparently only a small percentage of patients exhibiting coffee spots ever acquire neurofibromas.

DR. MEYER L. NIEDELMAN: I agree with Dr. Butterworth about the inadvisability of doing a biopsy. The clinical picture is so clearcut and distinct that this is not necessary. There have been reports of ectodermal defects occurring in conjunction with this disease. I would hesitate to perform a biopsy in answer to the question because nothing would be gained. I believe the patient will eventually acquire more lesions. He has manifested small fibromatous lesions on his legs in the past few months. The parents wish to know whether the mass on the left shoulder should be surgically removed, as it is conspicuous and painful. I would advise having it removed, surgically.

Macular Atrophy Occurring in Congenital Syphilis Five Years After Treatment.
Presented by DR. THOMAS BUTTERWORTH.

W. A., a white man aged 21 years, presents oval, ballooned and crinkled atrophic macules on the sides of the neck, shoulders and arms. He had bilateral interstitial keratitis, beginning in August 1938. There was confirmatory serologic and clinical evidence of congenital syphilis. Between October 1938 and January 1941 the patient received 44 injections of neoarsphenamine, 60 injections of bismuth subsalicylate and 12 injections of milk protein. On the occasion of his annual check-up in December 1946 atrophic macules were noticed around the neck and on the upper portion of the arms. His mother had syphilis.

The physical examination revealed no abnormality except the remains of interstitial keratitis. The vision was found to be 2/100, corrected to 20/40, in each eye.

Reactions to annual Kline and Kolmer tests for syphilis have varied from weakly positive to strongly positive. The spinal fluid gave a negative reaction in 1939. A recent blood count gave readings that were within normal limits.

The report on the biopsy was as follows: "There was a noninflammatory superficial edema of mild grade, together with a suggestive dilatation of the orifices of hair follicles. Certainly there were not any cellular infiltrations which would suggest syphilis or, for that matter, other inflammatory disease. The elastic tissue stain showed that elastic tissue fibers were

few and far between and what there were were highly fragmented. This observation clinched the diagnosis of macular atrophy." (Dr. Fred D. Weidman.)

The patient was treated with 6,000,0000 units of penicillin in December 1949.

DISCUSSION

DR. M. H. SAMITZ: Were there any precursor lesions?

DR. FRED D. WEIDMAN: I think there is one there tonight. On the arm is an elevated and rather firm lesion, preceding the softening and degenerative stage.

DR. THOMAS BUTTERWORTH, Reading, Pa.: I administered treatment with the arsphenamines and bismuth. Since the patient responded well, he was not given malaria therapy. He comes back every year for a complete check-up. In 1946 he showed me a few lesions on the leg, which I thought were Schweninger-Buzzi disease. He came back next year with more. If these lesions are due to syphilis, then we must have some other explanation in this particular case, because Dr. Weidman did not report any infiltrative lesions, simply degeneration of the elastic fibers. One would think that after something like 44 injections of neoarsphenamine and 60 injections of bismuth the syphilitic process would be well controlled. I gave the patient penicillin simply to ease his mind. One does not find many references to macular atrophy occurring in congenital syphilis.

DR. BERNARD L. KAHN: I used to see 60 syphilitic children every week for many years, but I never have seen a case of macular atrophy in congenital syphilis.

DR. FRED D. WEIDMAN: Is macular atrophy in congenital syphilis seen commonly in adults, nowadays?

CAPTAIN R. L. GILMAN (MC), U.S.N.: I have seen cases, but not with any particular regularity; one sees them and recognizes the possibility, but they are not common.

DR. FRED D. WEIDMAN: When I saw the patient tonight, I thought the condition Schweninger-Buzzi disease. There was this elevated lesion on the forearm; I thought of macular atrophy only when I read the report on the section. I should like to ask those who see macular atrophy whether they think that clinically the condition could be the Schweninger-Buzzi disease.

DR. HERMAN BEERMAN: I do not believe I have seen more than three such cases in acquired syphilis. I should like to ask Dr. Butterworth whether this might be a Schweninger-Buzzi type of macular atrophy, because I thought the lesions elevated rather than depressed.

DR. THOMAS BUTTERWORTH, Reading, Pa.: About 1935 I presented before this Society a case of macular atrophy in a little girl of about 9 or 10 years of age. Two photographs of that girl are still used by Andrews in his book. Schweninger-Buzzi disease, of course, is just a primary idiopathic macular atrophy, but it is difficult to try to sustain a case of primary macular atrophy in the presence of syphilis. But suppose this patient had had a case of syphilis with serologic reversal; then we would consider the case another one of Schweninger-Buzzi disease. I think Schweninger-Buzzi macular atrophy follows the lines of skin cleavage.

DR. H. H. PERLMAN: Do the blood vessels show endothelial obliteration?

DR. FRED D. WEIDMAN: No.

Granuloma Inguinale; Carcinoma? Presented by DR. J. M. SCHILDKRAUT, Trenton, N. J.

D. M., a Negro woman aged 37 years, complains of a new growth of the external genitalia. She was seen by the presenter for the first time on Jan. 11, 1950. She claimed that the growth began about the early part of November 1949. The external genitalia presented an immense ulcerated granulomatous process. The left labium majus was greatly hypertrophied and had a raw, red, oozing surface covered, in part, by a grayish exudate. The right labium minus was tremendously edematous and protruded downward as a large, pedunculated mass extending to the rectum; at its base it also showed a red granulomatous ulceration. The vaginal wall was not affected. The pubic area was somewhat thickened and had several sinus openings which later discharged a moderate amount of creamy yellow pus. The inguinal glands were palpable but not greatly enlarged. There was an annular fibrous structure in the lower part of the rectum. The tentative diagnosis was granuloma inguinale.

Repeated smears for Donovan bodies were negative. The Wassermann and Frei tests gave negative reactions. A roentgenogram of the chest revealed no abnormality. The report on the biopsy of the left granulomatous mass (Jan. 11, 1950) read: "Microscopic examination showed decidely hyperplastic pigmented squamous epithelium. Masses of tumor made up of atypical squamous cells with pleomorphic and hyperchromatic nuclei were seen. Scattered mitoses and some poorly formed epithelial pearls were seen. Some tumor cells were noted in vascular channels, apparently lymphatics. The impression was that the lesion was squamous cell carcinoma" (Dr. H. Y. Tyler).

The biopsy report of Feb. 1, 1950, on a specimen from the left vulva was: "Microscopic examination showed skin with some epithelial hyperplasia. At one edge there was extensive ulceration with invasion by a tumor made up of masses and nests of atypical squamous epithelial cells. Nuclei were pleomorphic and hyperchromatic. Mitotic figures were present. Imperfect keratinization was seen" (Dr. H. Y. Tyler).

The patient was treated with streptomycin intramuscularly, 1 Gm. daily for three weeks (Jan. 11 through Feb. 1, 1950), and aureomycin, 1 Gm. daily, beginning Feb. 15, 1950. The entire mass has been reduced to about three fourths of its former size. The ulcerated surface has become grayish and cleaner and shows evidence of epithelization. The patient has received no active therapy in the past two weeks.

DISCUSSION

DR. J. M. SCHILDKRAUT, Trenton, N. J.: According to this woman's statement, the condition existed only six weeks prior to her coming to the tumor clinic, there thus being a total of 10 weeks' duration. There has been some improvement with streptomycin therapy, but my associates and I thought maybe the secondary infection had improved. The lesion is quite definite and distinct and seems to be fungating. Dr. Weidman saw the slide tonight, and he, too, is of the opinion that the lesion is an epithelioma.

DR. FRED D. WEIDMAN: Of course, our examinations are rather hurried under these circumstances, but the condition looked like squamous cell cancer to me. Of course, pseudoepitheliomatous hyperplasia is sometimes a very difficult condition to distinguish from cancer, and, personally, where the situation is such as it is here, I would want to sit down and study the section for perhaps half an hour before I gave a final opinion, and preferably I would use my own staining technic, performed in my own laboratory. There is a great deal in the use of that method when one is deciding between pseudoepitheliomatous hyperplasia and squamous cell cancer; sometimes a little tinctorial difference will swing one definitely to one side of the question. But certainly there is a massive squamous cell hyperplasia deep down in the bottom of the section which looks very much like squamous cell cancer.

DR. CARMEN C. THOMAS: I would recommend surgical excision of the hypertrophied labia, which would accomplish the double purpose of relieving this patient of her discomfort from mechanical causes and of furnishing another adequate biopsy specimen. We have had four patients with granuloma inguinale within the past three years who, after having received adequate streptomycin therapy, had plastic correction of their tremendously hypertrophied vulvar masses, with beautiful healing and no relapse.

DR. HERMAN BEERMAN: This is a particularly interesting subject to me. I have managed to collect over 90 histological specimens on granuloma inguinale. Among these I am particularly interested in the epithelial changes, which range from ulceration to a picture of almost epitheliomatous character. Unfortunately, that fact does not help in the present situation because, although Philpott has reported pseudoepitheliomatous hyperplasia in this disease, we have had one patient who had streptomycin therapy, was given the diagnosis of granuloma inguinale and carcinoma and suffered amputation. Another patient in the Philadelphia General Hospital had a case of a similar type. A recent article in *The British Journal of Venereal Diseases* reports even basal cell carcinoma in such a disorder, which observation is a little difficult to understand. But the pictures are there. We have exactly the same problem at the University Hospital now, in a woman whose slide Dr. Weidman said showed definite prickle cell carcinoma, and in whom we found Donovan bodies, and whose slide was seen by the general pathologist, Dr. Horn, who took a more conservative stand, suggesting treatment with streptomycin and perhaps surgical operation. I think this problem is a greater one

than we realize from seeing just one patient. It is becoming more and more of a problem since people are becoming more alert to this disease.

CAPTAIN R. L. GILMAN (MC), U.S.N.: Is there any reason why surgical operation should not be done at this time?

DR. M. H. SAMITZ: I think the surgical approach would be much more radical if we conclude that we are dealing with a malignant growth. It is imperative to establish a diagnosis. Eliminate the possibility here of a prickle cell carcinoma. Another biopsy should be performed by the surgeon and, if necessary, a frozen section should be made.

DR. J. M. SCHILDKRAUT, Trenton, N. J.: These specimens were taken by surgeons.

DR. BERNARD L. KAHN: Couldn't the two conditions coexist?

CAPTAIN R. L. GILMAN (MC), U.S.N.: Yes, but that possibility does not help us.

DR. J. M. SCHILDKRAUT, Trenton, N. J.: We made smears and scrapings and have not found Donovan bodies. Would the streptomycin destroy them?

DR. M. H. SAMITZ: Not necessarily. We have found Donovan bodies after apparent clinical cure. It is Dr. Beerman who finds them for us.

LOS ANGELES DERMATOLOGICAL SOCIETY

Jud R. Scholtz, M.D., *President*

Molleurus Couperus, M.D., *Secretary*

Jan. 10, 1950

A Case for Diagnosis: Mesodermal Nevus? Presented by DR. NELSON PAUL ANDERSON.

A. R., a white woman aged 38, has had a group of symptomless lesions in the left lumbar region for the last eight years, consisting of 20 to 30 elevated large papular and nodular, relatively soft yellowish lesions. Biopsy was made of one of these lesions.

DISCUSSION

DR. KENNETH STOUT: The lesions, I believe, are nevoid and probably examples of epidermal nevi. Microscopically the epidermis showed the structure of seborrheic keratosis.

DR. L. H. WINER: I thought that histologically the condition resembled epidermal nevus. Sometimes one might attempt to differentiate this disorder from seborrheic keratosis by the presence in such a nevus of more keratin in proportion to the epithelial proliferation, there being in seborrheic keratosis more epithelium and less keratin. Of further interest were the changes in the papillary bodies of the cutis. These bodies were so edematous that we thought we were dealing with myxedema. Specially stained sections showed that the connective tissue in the papillary cutis had not attained its characteristic development. These collagen fibrils stained faintly and were much narrower than normal, simulating embryonic connective tissue. We see here a nevus consisting of both epithelial and connective tissue.

DR. A. FLETCHER HALL: The location is that in which mongolian spots are frequently found, and it may be that this particular region on the sacral area is prone to develop nevoid lesions of the mesoderm.

DR. NELSON PAUL ANDERSON: I thought when I first saw this condition that it was a papular myxedema. I would be willing to accept the diagnosis of a mesodermal nevus. It is difficult to believe that the disorder belongs in the group of epithelial nevi, although there may be that element in it.

Lichen Sclerosus et Atrophicus with Bleb Formation. Presented by DR. SAMUEL AYRES JR. and DR. SAMUEL AYRES III.

H. B., a white woman aged 63, has had an eruption for three years. On Dec. 23, 1949, the appearance was as follows: Lesions were scattered on the chest and were also present about the vulva and postanal areas. On the chest were three relatively noninflamed lesions, the largest approximately twice the size of a nickel, irregular and vertically oval. These

lesions had a white, scarlike appearance with slight scaling and were soft to the touch. On the right side of the chest just in front of the shoulder and below the clavicle was another vertical scarlike lesion, the upper portion of which was denuded and slightly crusted. The cicatricial portion had a somewhat lichenoid appearance. Between the breasts was an approximately quarter-dollar-sized lesion almost entirely covered by a large erythematous bleb or bulla with a smaller adjoining bleb. On the lower portion of the left breast was a transversely oval, irregular lesion about 3 inches (7.5 cm.) long and 1 to 1½ inches (2.5 to 4 cm.) wide, showing red scar tissue with a dime-sized to nickel-sized denuded portion. There were several small outlying pea-sized, slightly scaly, atrophic lesions. The vulva today shows a diffuse, erythematous, whitish and raw appearance. On the medial aspects of the upper portions of the thighs are several well defined, dime-sized to nickel-sized whitish, lichenoid and atrophic macules. The postanal intergluteal fold reveals a similar appearance.

The microscopic picture is considered diagnostic of lichen sclerosus et atrophicus.

DISCUSSION

DR. A. FLETCHER HALL: The lesions under the breasts suggest the possibility of Senear-Usher disease; even some of the lesions that were not bullous could fit into that category, but I believe that the diagnosis should be decided on histological grounds.

DR. PAUL D. FOSTER: I wondered whether Dr. Ayres considered the possibility of dermatitis factitia on the lesions under the breasts.

DR. WILLIAM E. MULVEHILL: I believe that on clinical grounds the diagnosis of lichen sclerosus et atrophicus can be accurately made, but the bullae, it seems to me, can be explained by the friction of the woman's clothing.

DR. WALTER F. SCHWARTZ: I agree with the diagnosis as presented. The only feature which would appear unusual is the presence of bullous lesions on the plaques on the glabrous skin. When this disease affects the mucous membranes, especially the vulva, bullae are not uncommon. The increased moisture under the breasts undoubtedly has played a part in the development of the bullae on the glabrous skin.

DR. SAMUEL AYRES JR: I thought this case interesting because I don't recall ever having seen this disorder on the glabrous skin with bullae before. I think probably the element of friction and trauma does play a role. The patient says the lesions itch. I have seen her three times, and each time there are new bullae. Along the vulva and upper inner aspect of the thigh are very typical lesions of lichen sclerosus. One rather interesting point Dr. Mirovich has pointed out is that freezing with solid carbon dioxide is very beneficial in some cases of lichen sclerosus et atrophicus. In view of the fact that the epidermis seems to split, I would be doubtful about trying that treatment in this case, however. Under the microscope there apparently was cleavage along the epidermal-dermal junction. Apparently the disorder is almost like a Nikolsky phenomenon. We are treating the patient with estrogenic hormones.

Tuberculoid Leprosy with Sudden Exacerbation While Patient Was Under Diasone® Therapy. Presented by DR. A. FLETCHER HALL.

DISCUSSION

DR. M. E. OBERMAYER: From the appearance of the color reproductions of the lesion and the clinical and laboratory observations, it is clear that this patient has tuberculoid leprosy. The presence of anesthesia on the surface of the annular plaque on the forearm is likewise in favor of a diagnosis of the tuberculoid form; lepromatous lesions are as a rule not anesthetic. Both the early and the late reactions to lepromin are strongly positive, and the microscopic sections showed the tuberculoid type of tissue reaction. The only anomalous feature is the observation of Mycobacterium leprae in relative abundance. In the typical tuberculoid lesion none or only very few organisms can be demonstrated. The explanation is that we are dealing here with a "reactive tuberculoid" patient. I nevertheless believe that the prognosis is good. As to the treatment, it is possible that the administration of diasone® (disodium formaldehyde sulfoxylate diaminodiphenylsulfone) has had an unfavorable influence on the course of the disease. Dr. Latapi, whom I visited recently, expressed the opinion that patients who have the tuberculoid form of leprosy sometimes react badly to the administration of the sulfones. He has used calciferol in such instances with good results. I suggest that this drug be given a trial.

Senear-Usher Pemphigus: Apparently Good Therapeutic Results from Aureomycin. Presented by DR. JUD R. SCHOLTZ and DR. CRAIG WILLIAMSON (by invitation).

The patient is a 22 year old white American man. He was presented before this Society early in 1949, at which time there was general agreement on the diagnosis. He was presented again in May 1949, shortly after sulfapyridine had been administered, at which time the patient felt that some improvement had followed the use of sulfapyridine.

In May 1949 treatment with aureomycin was begun, and during the succeeding three months the patient received a total of 29 Gm. of aureomycin and 4.5 Gm. of chloramphenicol (chloromycetin®), given in courses of five days each, with sulfapyridine being given concurrently with some of the courses. Within one week after the beginning of aureomycin therapy there was a striking change in the picture, and from that time the improvement has been steady and definite. No new lesions have appeared since August 1949, and all the old lesions have gradually healed, leaving some residual pigmentation. The lesions of the face were the last to heal. The patient is presented to show the results of treatment.

Senear-Usher Pemphigus Treated with Aureomycin. Presented by DR. MOLLEURUS COUPERUS.

I. Z., a Jewish male aged 62, born in the Russian Ukraine, has had a bullous eruption for eight years. He has been under observation at the Vanderbilt Clinic in New York for six years. He has shown more improvement with the administration of aureomycin, 500 mg. every six hours, than with any other form of therapy. He has taken a total of 500 capsules of 250 mg. each. The bullous lesions do not completely disappear with this treatment, but they are decidedly diminished in number. Tonight the patient has three bullous lesions.

DISCUSSION OF PRECEDING TWO CASES

DR. NELSON PAUL ANDERSON: There has been a lot of loose talk about aureomycin. First is that concerning its so-called beneficial effect on herpes zoster. At the present time there is an article in *The Journal of the American Medical Association* based on two cases of this disorder. I think personally that use of aureomycin in zoster is a waste of both money and aureomycin. Dr. Scholtz's patient certainly has shown a quite remarkable response to the drug. However, I hope no one will draw conclusions as to the so-called virus etiology of pemphigus, as I think doing so would be erroneous. There have apparently been some cases of widespread molluscum contagiosum which have responded to treatment with aureomycin given by mouth. As far as I know, this last-mentioned condition is the only true virus disease of the skin in which aureomycin has been of value. The fact that aureomycin has helped the condition of Drs. Scholtz and Williamson's patient and certain cases of dermatitis herpetiformis is well established, but to draw the conclusion that these disorders are virus diseases, I think, would not be justified.

Tinea Capitis (Microsporum Lanosum) in a Woman Aged 72. Presented by DR. J. WALTER WILSON.

R. R., a 72 year old woman, a year ago noticed on her face a few reddened spots which were extremely pruritic. This eruption slowly spread to involve her neck, nape, scalp and sternal area. Several doctors made the diagnosis of "ringworm" and prescribed various salves. The patient has never owned or handled pets and is not exposed to children. The menopause occurred 30 years ago.

Six months ago it was demonstrated by culture that the infection was due to Microsporum lanosum. Examination of the scalp under filtered ultraviolet radiation (Wood's light) revealed numerous hairs fluorescing strongly, principally in the manner typical of children's scalps involved with this infection, but, in addition, some long hairs were observed which exhibited fluorescence only near their follicular insertion. Treatment with 5 per cent salicylanilide and 15 per cent copper undecylenate in carbowax® 1500 has ameliorated but not cured the condition. The patient refused to clip the hair closely until recently, and there was a period of perhaps two months when no treatment was applied because she was ill with a cardiac condition.

DISCUSSION

DR. SAMUEL AYRES JR.: This case simply shows that the sex hormones apparently create an immunity to ringworm of the scalp. After cessation of menstruation the scalp again becomes susceptible. If there is any difficulty in curing the disease, perhaps the use of estrogenic hormones by mouth or locally would facilitate the matter.

DR. WALTER SCHWARTZ: I think this is the third case in adults shown here in the last two years. One of the patients was postmenopausal; the other was only 33 but gave some vague history of menopausal disturbances. I have seen one patient in my practice with tinea capitis during pregnancy. There undoubtedly must be some endocrine factor present which makes these adults susceptible to the infection.

A Case for Diagnosis: Lichen Sclerosus et Atrophicus? Balanitis Xerotica Obliterans? Presented by DR. SAMUEL AYRES JR. and DR. SAMUEL AYRES III.

A Case for Diagnosis: Colloid Degeneration of the Skin? Basal Cell Epithelioma? Presented by DR. J. WALTER WILSON.

A Case for Diagnosis: Fixed Drug Eruption? Presented by DR. SAMUEL AYRES JR. and DR. SAMUEL AYRES III.

Generalized Sarcoidosis in a White Woman. Presented by DR. PAUL D. FOSTER.

Generalized Sarcoidosis(?) in a White Woman. Presented by DR. PAUL D. FOSTER.

Solar Eczema with Beginning Lupus Erythematosus of the Face. Presented by DR. PAUL D. FOSTER.

Phagedenic Chancroid? Presented by DR. ANKER K. JENSEN.

A Case for Diagnosis: Phrynoderma? Presented by DR. KENNETH L. STOUT.

Melanoma (?) of Right Cheek: Patient Presented for Therapeutic Suggestions. Presented by DR. MAXWELL J. WOLFF.

A Case for Diagnosis: Fixed Drug Eruption? Lupus Pernio? Erysipelas Perstans Faciei? Presented by DR. WALTER F. SCHWARTZ.

Jud R. Scholtz, M.D., *President*

Molleurus Couperus, M.D., *Secretary*

Feb. 14, 1950

Hydroa Aestivale, Treated with Estrogens. Presented by DR. PAUL D. FOSTER.

L. F., a white girl aged 8, has had frequent attacks of dermatitis since the age of 9 months. I saw her first when she was at the age of 6½ years, on June 17, 1948, at which time she presented multiple depressed scars and clear vesicles and bullae with pronounced crusting on the face, arms and hands. The hair was very thin and broken off short. A biopsy taken at the time of her first visit was not deep enough to permit a diagnosis. The family history revealed no other cases of this disease. Treatment has consisted of 24 injections of aqueous estrone, 0.2 cc. There is at present practically a complete cessation of symptoms.

DISCUSSION

DR. SAMUEL AYRES JR.: It is difficult to recognize hydroa aestivale without active lesions. It seems to me there is a thyroid deficiency here. The child has almost the appearance of a cretin. The fingers are stubby, and something about the eyes, heavy features, dry skin and thin hair suggest thyroid deficiency. I would have roentgenograms taken of the hands and wrists to determine whether there is any delay in ossification. I believe the child has had treatment with thyroid substance as well as estrone, and perhaps the beneficial results are due to the thyroid substance.

DR. PAUL D. FOSTER: When I first saw this girl, I made the diagnosis of hydroa aestivale because the lesions were definitely vesicular and limited to the exposed areas of the face, neck and lower arms. On the child's avoidance of sunlight the lesions gradually cleared, and then they recurred when she was again exposed to the sun. It is true that the fingers do appear scarred as in epidermolysis bullosa. I have treated this patient for three years, first with thyroid and posterior pituitary (pituitrin®) with no appreciable change. I have followed Dr. Lain's program with 500 units of estrone weekly, and since this therapy was begun, approximately six months ago, the condition has cleared up completely, the patient having had no vesicles or erythematous lesions of any type for the past four months.

Hypertrophic Lichen Planus of Legs (Popliteal Spaces): Patient Presented for Therapeutic Suggestions. Presented by DR. NELSON PAUL ANDERSON.

DISCUSSION

DR. MAXWELL J. WOLFF: I would treat the patient with solid carbon dioxide, applied locally for eight or 10 seconds once a week for five or six weeks.

DR. SAMUEL AYRES JR.: I think some cases are probably kept active by other factors. This man's teeth are in bad shape, and he has one broken root. I would make sure he had a complete dental roentgenologic study. I think any chronic infection can keep lichen planus going. I have had several patients that for some unknown reason have shown good response to treatment with a high potency vitamin B complex preparation with ascorbic acid, together with vitamin A. Perhaps that would be worth while in this case. Finally, it might be of value to paint some pure coal tar over the lesions and dust them with talcum as one would in chronic neurodermatitis.

DR. M. E. OBERMAYER: When lichen planus is limited to the presence of a few chronic hypertrophic plaques, systemic therapy is of little avail. Local protection by the application of flexible collodion to which 5 per cent heliobrom® powder (urea dibromtannate; Doak) has been added is sometimes useful because it helps to prevent the damaging effect of constant scratching.

Gumma of Tongue. Presented by DR. HARRY LEVITT and DR. NORMAN E. LEVAN (by invitation).

W. D. M., a 61 year old white man, has had a "sore" on his tongue for one year. There is no history of primary or secondary syphilis. The lesion on his tongue has gradually increased in size and has been relatively painless. At present there is a destructive lesion, with a serpiginous border, involving much of the left side of the tongue. There is a rubbery 2.5 cm. submandibular mass on the left side of the neck. No other physical observations suggesting syphilis are present. The Kahn and Kolmer serologic tests for syphilis gave strongly positive reactions, while observations on spinal fluid examination were normal. The patient has received three intramuscular injections of 2 cc. of bismuth subtartrate during the last two weeks, and there has been a noticeable improvement in the tongue lesion.

DISCUSSION

DR. WALTER SCHWARTZ: There is a positive serologic reaction and a strong history of syphilis, but even so I feel strongly that a diagnosis of active gummatous lesion cannot be made. Gummatous lesions usually do not progress this far without some evidence of spontaneous healing, with deep scar formation. Here there is a deeply destructive lesion with no evidence of healing anywhere. The lesions are apparently quite infiltrated at the margins. The patient has palpable maxillary lymph nodes, and in the absence of biopsy one should suspect squamous cell carcinoma of the tongue. I recommend a biopsy.

NOTE.—A biopsy taken from the tongue lesion revealed squamous cell carcinoma.

A Case for Diagnosis: Darier's Disease? Pityriasis Rubra Pilaris? Presented by DR. MAXWELL J. WOLFF.
Glossodynia. Presented by DR. SAMUEL AYRES JR.
A Case for Diagnosis: Dermatitis Atrophicans Maculosa? Presented by DR. FRANKLIN I. BALL.
Necrobiosis Lipoidica Diabeticorum? Granuloma Annulare? Presented by DR. LAWRENCE M. NELSON.
Beckhart's Impetigo, Successfully Treated with Aureomycin Given by Mouth. Presented by DR. H. C. L. LINDSAY.
Ritter's Disease, or Dermatitis Exfoliativa Neonatorum. Presented by DR. PAUL D. FOSTER.
Pernio (Chilblains). Presented by DR. SAMUEL AYRES JR.

SAN FRANCISCO DERMATOLOGICAL SOCIETY

Robert A. Stewart, M.D., *President*

Rees B. Rees, M.D., *Secretary-Treasurer*

Feb. 24, 1950

Solid Edema of the Face. Presented by DR. EDWARD J. RINGROSE and DR. GORDON H. EKBLAD.

J. J. M., a 33 year old white man, first became aware of a change in his face in August 1949. This has increased very slowly in extent. A photograph taken in 1946 is shown for

comparison. There is no history of recurrent erysipelas-like infection. The involvement is asymptomatic. The patient received 1,000,000 units of penicillin in the fall of 1949, with no apparent benefit. There is brawny nonpitting swelling over the nose, the right maxillary area and the right periorbital area medially. There is no erythema or pigment deposition. Results of laboratory studies, including routine blood examination and urinalysis, basal metabolic rate determination, electrocardiograms and roentgenologic examination of the sinuses and chest as well as the entire gastrointestinal tract, were noncontributory. Histologically there were areas of homogenization of the collagen and a stain for mucin gave negative observations. There was edema of the corium. Hair follicles and sebaceous glands were present. The vascular structures were normal. There was a moderate diffuse infiltrate, chiefly of lymphocytes. The patient has received two injections of hyaluronidase in the area about the biopsy scar, with apparently some improvement in this area. He has received two injections of hyaluronidase over the left side of the nose, with no apparent benefit.

DISCUSSION

DR. FREDERICK G. NOVY JR.: The fact that there are 15,000 leukocytes in the blood count is important and should be investigated further. I think that another antibiotic should be tried.

DR. REES B. REES: Some years ago Dr. New and his associates at the Mayo Foundation suggested the use of boiling water by injection for this condition. They mentioned that repeated injections over a period of years might be necessary and that this treatment should be followed with radium therapy. I have had no personal experience with this method but have had the opportunity to see a patient in consultation with an ophthalmologist, the patient's lesions involving the right eyelids. This treatment was cautiously tried by the ophthalmologist, and apparently there was some success.

DR. EUGENE FARBER: The treatment advocated by Dr. New is very uncomfortable. The operators have to be very careful, and this requires much skill. There may be a slough in the muscle, with resultant disfigurement.

DR. FREDERICK G. NOVY JR.: In one case radiation was tried with copper filtration, with no response.

Cavernous Hemangioma. Presented by DR. EDWARD J. RINGROSE and (by invitation) DR. PATRICK BUTLER.

Mrs. W. M., a 30 year old white woman, has had a tumor mass over the right zygoma all of her life. This has enlarged during the past 10 years with more pronounced growth during the past year. The lesion may flush for two days at a time. An occasional sharp pain occurs. The mass changes in size on change in position and at times seems to clog up and become lumpy. In December 1948 the patient was given two injections locally by a physician in Fort Smith, Ark. These were not painful, but the eye turned black and became swollen after the second one. A mottled bluish brown tumor mass, roughly 2 inches (5 cm.) in diameter, is present over the right zygoma lateral to the right eye. Dilated blood vessels are seen to extend from the lesion to beneath the right eyelid.

DISCUSSION

DR. WILLIAM D. MCCARTHY (by invitation): This is a very interesting case in many respects. Particularly interesting is the patient's history that the angioma developed during her first pregnancy. This is further support for our observation in a large series of cases published in *Surgery, Gynecology and Obstetrics* (November 1940) that many angiomas in adults are stimulated during pregnancy and the menarche.

This particular cavernous hemangioma should be treated soon because of its proximity to the temporal artery. One of our patients with an angioma in the same location manifested a pulsating arteriovenous mass when the temporal artery suddenly established a communication. The pulsating hemangioma eroded into the antrum and orbit, destroying the eye, and was controlled only by surgical ligation. In this case presented by Dr. Ringrose we could consider a trial of a conservative course of sodium morrhuate injections or implantation of gold radon seeds. However, the preferred treatment is surgical.

DR. ROBERT LOFGREN: I should like to ask Dr. McCarthy what the theory or explanation is for progression of these lesions during pregnancy.

DR. WILLIAM D. MCCARTHY (by invitation): The phenomenon is apparently a hormonal phenomenon and is related to the estrogen levels.

DR. ROBERT LOFGENR: That would be a probable explanation. Estrogen is a vasodilator and is considered the causative factor in various circulatory phenomena of pregnancy.

A Case for Diagnosis: Pemphigus? Pemphigus Erythematosus? Presented by DR. NORMAN EPSTEIN and DR. JAMES R. ALLEN.

D. B., an elderly white man, first acquired bullae 10 months ago on the vertex and frontal area, spreading over the face and the lateral surfaces of the neck. New lesions start as red areas with a blister which slowly develops, lasting one week with crust formation. This spot becomes very pruritic and seems to leave a scarred white area. In 1939 a mass was treated in the esophagus, the biopsy showing an inflammatory lesion with many plasma cells. When the patient was first seen by us, on Feb. 20, 1950, there were discrete red scaling lesions, some with central flaccid bullae. Others were crusted, and older lesions were depigmented with some atrophic scarring. They were scattered over the face, the nape and the bald pate. Mucous membranes are clear. Results of routine urinalysis and blood count were noncontributory. A biopsy specimen of the left side of the neck showed focal hyperkeratosis, degeneration of the epidermis with separation from the dermis and organizing inflammatory reaction in the dermis.

DISCUSSION

DR. JULES KEY: There are no blisters present today, but the patient gives a history of having bullae in the past, and he does have a positive Nikolsky sign. I think that this is a case of pemphigus.

DR. EUGENE FARBER: I feel that I should argue in favor of bullous lupus erythematosus. The plaques show spotty atrophy in section. This picture is most unusual. In addition, the silvering of the lip is of interest.

DR. GRANT MORROW: I suggest pemphigus erythematosus.

DR. REES B. REES: I agree with Dr. Morrow's remark. I saw this patient some time during the past year, and he had bullae only at that time.

DR. NORMAN EPSTEIN: I lean more toward the diagnosis of bullous lupus erythematosus. It is unusual for lupus erythematosus to start at such an advanced age. It is also unusual for pemphigus to remain limited to the face and scalp.

A Case for Diagnosis: Lichen Planus? Pseudo Lichen Planus Due to Quinacrine Hydrochloride? Presented (by invitation) by LIEUTENANT COLONEL JOSEPH T. CAPLES, Medical Corps.

Keratosis Pilaris? Darier's Disease? Presented by DR. EDWARD J. RINGROSE and DR. GORDON H. EKBLAD.

Lupus Vulgaris. Presented by DR. OTTO E. L. SCHMIDT and (by invitation) DR. WALTER J. COLE.

Syringoma or Epithelioma Adenoides Cysticum. Presented by DR. ARNE INGELS.

A Case for Diagnosis: Leukoderma Acquisitum Centrifugum? Presented by DR. EDWARD RINGROSE.

A Case for Diagnosis: Lymphocytoma? Localized Form of Spiegler-Fendt Sarcoid? Presented by DR. EDWARD RINGROSE and DR. G. H. EKBLAD.

Parapsoriasis. Presented by DR. FRANCES KEDDIE.

Persistent Urticaria Following Penicillin Therapy, of Seven Months' Duration. Presented by DR. ERVIN EPSTEIN.

Lymphoblastoma (Mycosis Fungoides, Vidal and Brocq Type?). Presented by DR. FRANCES TORREY and DR. CHARLES CASKEY.

Multiple Superficial Basal Cell Epithelioma. Presented by DR. EDWARD LEVIN.

Atopic Dermatitis. Presented by DR. GEORGE LENAHAN.

Correspondence

LETTER FROM THE GERMAN DERMATOLOGICAL SOCIETY REGARDING THE DEATH OF DR. FRED WISE

Munich, November 17, 1950,
Dermatological clinic of the University,
Frauenlob Street 9.

Dr. Henry E. Michelson,
President of the American Dermatological Society,
Medical Arts Building,
Minneapolis, Minn.
My dear Colleague,

I have just learned that the outstanding American dermatologist Fred Wise died in July 1950.

Dr. Wise was held in high esteem by the German dermatologists, as can be [proved] by the fact that he was one of the few foreigners mentioned in the 1929 German Calendar of Dermatologists with a list of his publications. I am expressing in the name of the German Dermatological Society my heartfelt sympathy in the loss of this great scientist. His entire lifework has enriched dermatology throughout the world. We feel your loss to be our loss too, and you will believe that we share your bereavement. What a void his departure has created!

Assuring you of my sincere regards and kindest greetings,
I remain,
Very truly yours,
A. MARCHIONINI, President
German Dermatological Society

News and Comment

GENERAL NEWS

Examinations by the American Board of Dermatology and Syphilology.—The spring examinations of the American Board of Dermatology and Syphilology will be held as follows: The written examinations are scheduled for April 5, 1951 in various cities throughout the United States. The oral examinations will be given in New York city on June 8, 9 and 10, 1951.

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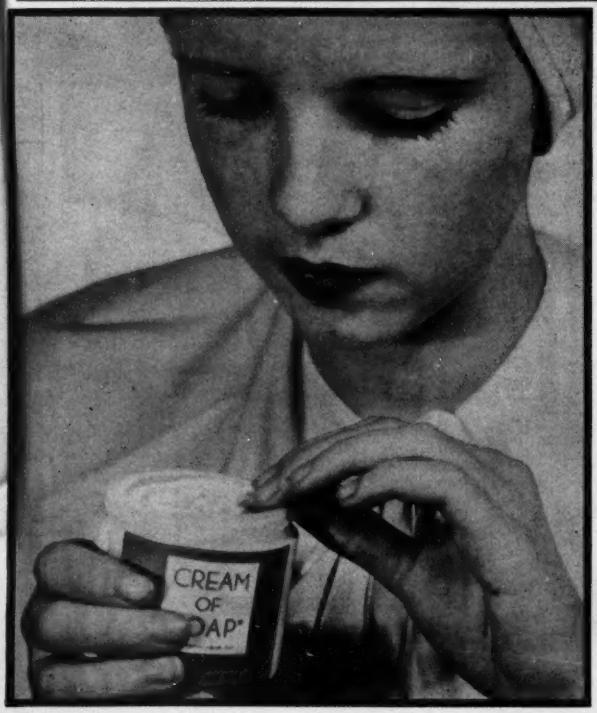

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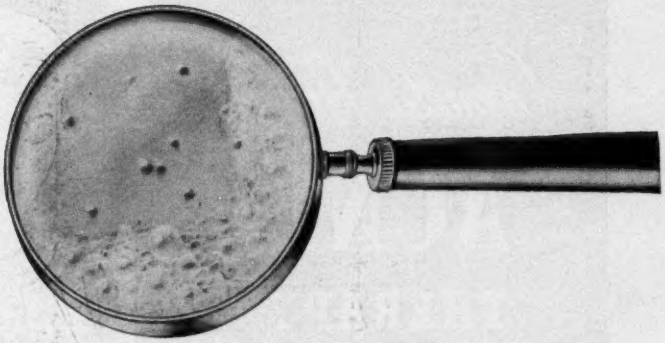

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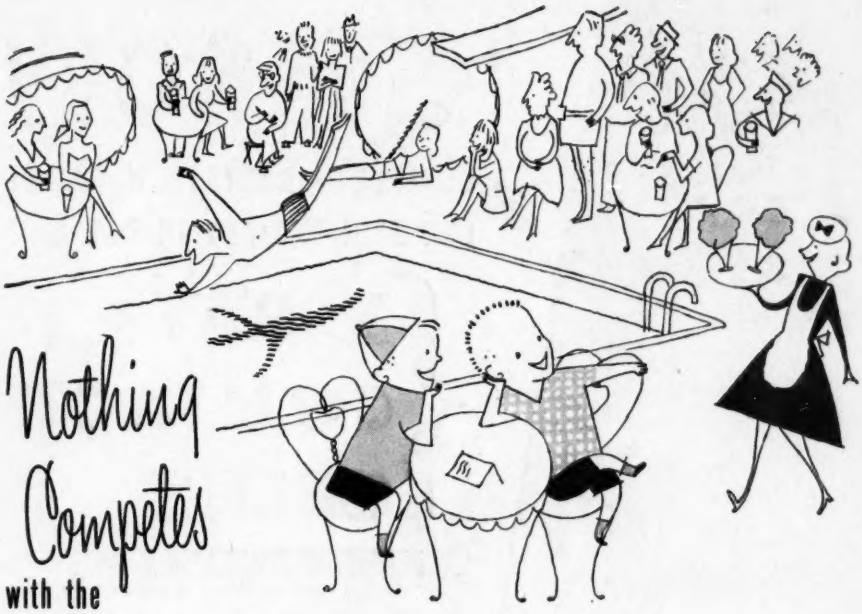

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1. Lehr, D. (1950), Relative Merits of Commonly Used Sulfonamide Drugs as Components of Mixtures, N. Y. State J. Med., 50:1361, June.

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